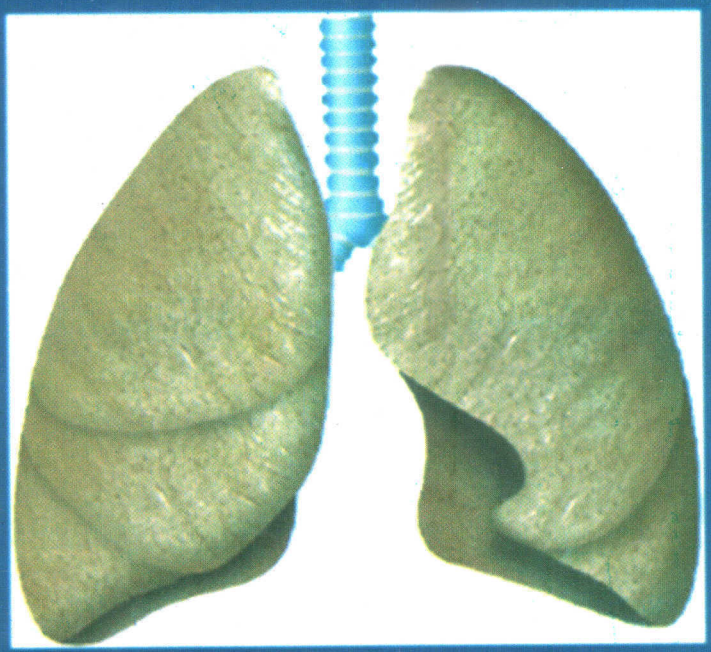
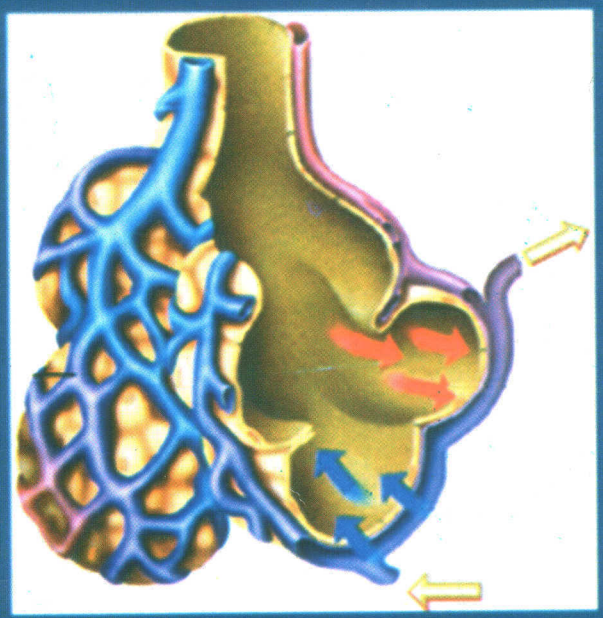
LECTURE NOTES OF INTERNAL MEDICINE

Respiratory Diseases





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Anatomy and Physiology of the Respiratory System

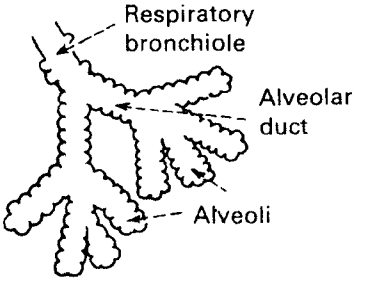
- The upper respiratory tract includes the nose, nasopharynx and larynx. It is lined by vascular mucous membranes with ciliated epithelium on their surface.
- The lower respiratory tract includes the trachea and bronchi. It is lined by ciliated epithelium. The trachea is 10-12 cm in length, it lies slightly to the right of the midline and divides at the carina into right and left main bronchi. The carina lies under the junction of manubrium of the sternum and the second right costal cartilage. The right main bronchus is more vertical than the left and, hence inhaled material is more likely to pass into the right lung.
- The functions of nasal breathing are, to heat, moisten the air and remove particulate matter.
- The larynx and large bronchi are rich in sensory receptors involved in the cough reflex.
- The alveoli are lined with flattened epithelial Cells **(type I pneumocytes)** and cuboidal cells (**type II pneumocytes)**.
- Type II pneumocytes can divide and reconstitute type I pneumocytes after injury. Also they produce the surfactant which reduces the surface tension of the alveolar wall to prevent collapse.
- There are about 300 million alveoli in each lung, their total surface area is 40-80m^2

Bronchial tree and the respiratory acinus:

- The large bronchi divide into smaller bronchi which divide into small bronchioles then terminal bronchiole then respiratory bronchioles.
- The respiratory bronchioles may branch 3-5 times.
- Eventually the respiratory bronchioles form alveolar ducts then alveoeli. Each respiratory bronchiole supplies about 200 alveoli via the alveolar duct.
- The fundamental unit of the lung is the respiratory acinus which is the part of lung tissue formed by the branching of a single terminal bronchiole as above.

Nerve supply to the lung:

- The parasympathetic supply is from vagus and the sympathetic from the sympathetic chain.
- The parietal pleura is innervated from intercostal and phrenic nerves while the visceral pleura has no innervation.



Normal

Control of respiration

- Discharges arising form respiratory center in brain stem travel via the phrenic and intercostal nerves to the respiratory musculature leading to coordinated respiratory movement.

✪ **Neurogenic and chemical factors are involved in the control of respiration:**

Neurogenic factors:

- ✪ Impulses from limb receptors as muscles and joints, stimulated by exercise.
- ✪ Impulses form pulmonary receptors sensitive to stretch and irritation, stimulated in asthma, pulmonary embolism, pneumonia.
- ✪ Juxtapulmonary capillary receptors (J receptors) stimulated by pulmonary venous congestion.

Chemical factors:

- ✪ The respiratory centre itself is sensitive to CO_2 and H+ ions in blood due to acidosis.
- ✪ Peripheral chemo-receptors in the carotid and aortic bodies sensitive to hypoxia.

Lung Defense

1. Particles removed from inspired air by the nose.
2. The larynx acts as sphincter during cough.
3. Mucociliary escalator of the trachea and bronchi (clearance of particles).
4. Protective agents in the lung lining fluids:
   i. Surfactant → bacterial opsonisation.
   ii. Immunoglobulin (IgA, IgG, IgE).
   iii. Complement, antioxidant (superoxide dismutase), interferon.
   iv. Lysozme is an enzyme found in granulocytes that has bactericidal properties.
5. Alveolar macrophages (derived from precursors in the bone marrow).
6. Protease inhibitor (α_1 antitrypsin) for protection of the host tissue during the inflammatory process. It inhibts chemotrypsin and trypsin.

Examination and symptoms → see clinical sheet.

Investigations of lung disease (see later for details)

- ☆ **X-ray,ECG, pulmonary angiography**.
- ☆ **Lung scan** (perfusion and ventilation scan).
- ☆ **Endoscopy** → laryngoscopy, bronchoscopy and mediastinoscopy.
- ☆ **CT scan**

Value of CT scan in chest diseases:

- •• Detection of an interstitial lung disease and its extent as in sarcoidosis, occupational Lung diseases and extrinsic alveolitis
- •• Diagnosis of early bronchiectasis.
- •• Distinguishing emphysema from interstitial lung disease.
- •• Diagnosis of lymphangitis carcinomatosa disease.
- •• CT scan is valuable in bronchial carcinoma staging to demonstrate mediastinal, pleural or chest wall invasion and to determine operability.

- **MRI**
  - **Useful in the differentiation of masses around the aorta or in the hilar regions.**
- **Pleural aspiration**.
- **Pleural biopsy** is of value to diagnose T.B.
- **Transbronchial lung biopsy** for diagnosis of some diseases, **e.g**. Sarcoidosis.
- **Respiratory function tests (see later)**.

Diseases and Infections of Upper Respiratory Tract

(1) Acute corysa (Common cold).

- It is a highly infectious disease.
- It is due to rhinovirus.
- The incubation period is 12 hours – 5 days.
- There is rapid onset of low-grade fever, burning sensation in nose, sneezing, sore throat, blocked nose with watery discharge eventually becoming thick and mucopurulant.
- Complications are sinusitis, lower respiratory tract infection e.g. bronchitis, pneumonia and otitis media.
- No specific therapy, most do not require treatment. Paracetamol 0.5 gm/6-8 hours and nasal decongestant for relief of systemic symptoms, no need of antibiotics in uncomplicated cases.

(2) Acute laryngitis.

- It is usually viral, it is manifested by hoarseness of voice, painful dry cough. Attempts to speak cause pain.
  Stridor in children.
- Complications are descending infection leading to tracheitis, bronchitis or pneumonia.
- It is treated by rest of voice, paracetamol 0.5 gm/6-8 hours, steam inhalation may be of value.

(3) Acute laryngo-tracheobronchitis (croup)

- It is caused by parainfluenza virus.
- It is manifested by paroxysms of cough associated by stridor and dyspnea.
- Cyanosis and asphyxia in children.
- It is complicated by Asphyxia.
- The treatment is by inhalation of steam, tracheostomy to relieve the obstruction, oxygen therapy and adequate fluids.

(4) Acute epiglottitis.

- It is caused by H. influenza causing swelling of epiglottis and the surrounding structures.
- It is manifested by stridor and cough in absence of much hoarseness.
- The complication is asphyxia.
- It is treated by I.V ceftazidime or chloramphenicol. Endotracheal intubation is usually needed.

Death from asphyxia may be precipitated by attempts to examine the throat. So, avoid using a tongue depressor or any instrument until facilities to maintain patent airways are available e.g. endotracheal intubation or tracheostomy.

(5) Influenza

Causes: Myxoviruses type A, B

I.P: 1-3 days.

C/P:

- Sudden onset of pyrexia, generalized aches, anorexia, nausea and vomiting.
- Symptoms usually subside within 3-5 days, but may be followed by post influenzal asthenia which may persist for several weeks.

Complications:

- Tracheitis
- Bronchitis
- Bronchiolitis
- Bronchopneumonia.

Secondary bacterial invasion by strep pneumoniae, H influenza and staph may occur.

- Toxic cardiomyopathy.
- Encephalitis.
- Demyelinating encephalopathy and peripheral neuropathy.
- Post influenzal asthenia.

Treatment:

- Bed rest until fever has subsided.
- Paracetamol 500 mg/6hrs.
- Antitussive.
- Specific therapy of pneumonia may be needed (see later).

Prophylaxis:

Vaccination especially for risky or susceptible people e.g.:

- Chronic heart disease.
- Chronic chest disease e.g. COPD, interstitial pulmonary diseases, bronchial asthma.
- Chronic renal failure.
- D.M
- Immunocompromised patients.

(6) Rhinitis

Rhinitis is present if sneezing attacks, nasal discharge or blockage occur for more than an hour on most days for a limited period of the year (**seasonal rhinitis**) or throughout the whole year (**perennial rhinitis**).

Seasonal rhinitis: (common in June and July)

It is often called (hay fever), it is the most common allergic disease. It is manifested by nasal irritation, sneezing and watery rhinorrhea. Itching of the eye and ears is common. Seasonal attacks of asthma and conjunctivitis may occur.

Perennial rhinitis:

Types:

- Allergic rhinitis
- Non allergic rhinitis.
- Vasomotor rhinitis (No demonstrable allergy) due to autonomic imbalance of the nervous system innervating the nasal mucosa.
- Nasal polyps, there is loss of smell and taste, sneezing is rare.

Treatment (Allergen avoidance) plus:

- Antihistamincs
- Decongestants
- Steroid nasal spray
- Sodium cromoglycate nasal spray

Acute bronchitis and tracheitis

- Often follows acute coryza.
- It is common in smokers and in patients with COPD (often pneumococci and H influenza).
- It also occurs in previously healthy persons (often viral).

C/P

- Irritating unproductive cough then productive cough with scanty mucoid sputum. After a day or so sputum becomes mucopurulant.
- Tracheitis leads to retrosternal discomfort and painful cough.
- Wheezing may occur.
- Rhonchi or crepitation that changed or disappear after cough may be present.
- Low grade fever may occur.

Investigations:

↑ TLC with ↑ neutrophil.

Complications:

- Bronchopneumonia.
- Exacerbation with development of type II respiratory failure in cases of severe COPD.
- Acute exacerbation of bronchial asthma and COPD.

Treatment (Spontaneous recovery occurs within few days).

- Specific treatment rarely necessary in previously healthy individuals, but it is essential in patients with COPD and in asthmatics.
- We can give amoxycilline 500 mg/6 hours, expectorants e.g. K-iodides plus paracetamol as an antipyretic if needed.

Obstructive lung diseases

Def. Group of diseases characterized by decrase the expiratory flow rate. The obstruction increased during expiration due to increase of intrathoracic pressure.

↓

This leading to prolonged active expiration.

i.e (Harsh vesicular breathing. (a common character of this group)

Types of obstructive lung diseases :

1- Chronic obstructive pulmonary disease (COPD)
   a-Chronic bronchitis
   b-Emphysema
2- Bronchial Asthma.
3- Bronchiectasis is considered as an obstructive and purulent lung disease.
4- Cystic fibrosis. 5-Asthmatic bronchitis!?

Asthmatic bronchitis is an old term but it can describe patient with chronic bronchitis +super imposed bronchospasm in association with inahled irritants or during respiratory infections.

Factors that determine the type of obstructive lung disease (Pathophysiology of airway obstruction)

(1) Chronic irritation

{ Smoke or Fumes } → Bronchial inflamation

↓

Chronic productive cough (chronic bronchitis)

(2) Bronchospasm (Triggered by antigenic or non antigenic stimuli).

↓

Paroxysmal attacks of dyspnea and wheezy chest **(i.e** bronchial asthma.**)**

(3) Chronic Irritation. + bronchospasm

↓

Asthmatic bronchitis**(**chronic bronchitis **+** superimposed bronchospasm**)**

(4) Diminished compliance and elasticity of the lung tissue

- This occurs with progressive distruction of alveolar walls as in cases of emphysema
- Since the expiration is a passive process that depends upon the elastic recoil of the lung So, emphysema leads to an expiratory air way obstruction → harsh vesicular breathing.

Chronic bronchitis / emphysema called COPD

Chronic obstructive pulmonary disease (COPD)

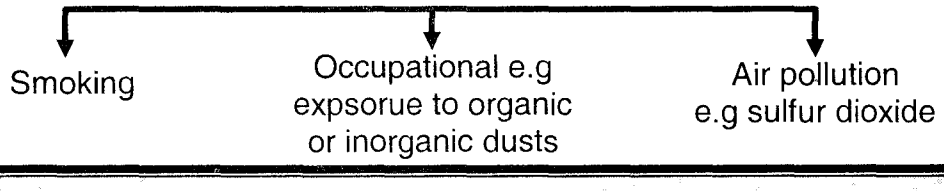
COPD is the internationally preferred term encompassing chronic bronchitis and emphysema. By definition COPD is a chronic slowly progressive disorder characterized by air flow obstruction (FEV_1 < 80% of the predicted value). The airflow obstruction is generally progressive, may be accompanied by airway reactivity and may be partially reversible.

Although pure form of chronic bronchitis or emphysema do exist, but still there is considerable overlap in the majority of patients so, it is better to use the term COPD in cases of chronic bronchitis/emphysema.

I Chronic Bronchitis

Def: It is a chronic disease of the bronchial tree characterized by excessive mucus secretion leading to productive cough on most days of at least 3 consecutive months for at least 2 successive years. Diagnosis requires exclusion of the other conditions associated with cough and sputum production e.g. bronchiectasis.

Causes: **(Chronic irritation)**



- Tobacco smoking in pack-years (the number of years has smoked X the number of packs smoked per day) is directly related to ventilatory dysfunction and pathologic changes in the lung.
- Smoking stimulates inflammatory cytokines and depresses alveolar macrophages, reduces the functional integrity of pulmonary surfactant, retards mucous transport, enhances the release of lysosomal enzymes, and produces other effects believed to be involved in the pathogenesis of COPD.

Q Role of respiratory tract infections:

- Viral or bacterial chest infections are considered as exacerbating factors rather than a cause.
- Also exposure to dampness, sudden changes in temperature and to fog leading to exacerbations.

Pathological stages: (Recent evidence suggest that COPD begins in the small airways).

1- Simple chronic bronchitis

Mucosal edema and congestion due to chronic irritation
with hypertrophy of mucous secreting glands and
↑ no of goblet cells of bronchial tree → ↑ mucous production

2- Mucopurulant (secondary infection) stage

The sputum is mucopurulant (during intercurrent infections), commonly by H-influenza or pneumococci.

3- Chronic obstructive stage.

This stage is due to peribronchial fibrosis, squamous metaplasia of bronchial epithelium and hypertrophy of bronchial muscle layer. This stage commonly associated with emphysema.

C/P

Sympt
- Age usually above 40 years
- Sex: male > female
- Cough: characterized by
  - Productive (see the definition)
  - Sputum
    - whitish
    - Mucoid
    - Small amount
  - Yellowish (during infection), more at the morning (up regulation of bronchial receptors at early morning + stored secretions !?)
- Dyspnea usually with emphysema or bronchospasm on top
- Chest pain due to chronic cough (intercostal muscle pain) or due to pneumothroax (rupture emphysematous bullae).
- Exacerbations may occur (on top of chest infection)

Examples of excacerbations :

(1) Patient with chronic bronchitis + emphysema with chest infection on top.

↓

Respiratory failure(dyspnea+cyanosis+deterioration of the level of consciousness)

(2) Chest infection in patients with COPD may manifested also with just cough by day and night, increased amount of sputum, discoloured sputum, fever or blood tinged sputum.

Sequences of COPD with age:
- In teenagers who smoke, mild asymptomatic changes develop in the small airways.
- As adults, there is chronic cough together with symptoms suggestive of an upper respiratory infection.
- By middle age, There is significant bronchial disease characterized by progressive airway obstruction that produces dyspnea on exertion which is unrecognized with sendentary lifestyle.
- Chest infections or surgery place the respiratory system under stress so the presence of COPD becomes evident (precipitating factors).

O/E

General Examination:

- Cyanosis with respiratory failure.
- Signs of cor Pulmonale → Congested neck veins
  → Lower limb edema
  → Congested liver (enlarged, tender)
- Neck veins showing expiratory filling with emphysema.
- Epigastric pulsations **(Rt. v++)**
- Puffiness of eye lids due to chronic cough.
- Clubbing ↓
- Pulse →↑ CO_2 → bounding pulse

It may occur due to hypoxia or with bronchiectasis or bronchogenic carcinoma on top .

Local examination:

Inspection: Symmetrical chest, limited movement on both sides.
↑ A-P diameter with emphysema.

Palpation:

- T.V.F. (equal on both sides)
- Palpable rhonchi.
- Epigastric pulsations due to right ventricular hypertrophy (Cor pulmonale).

Percussion: Hyper-resonance with emphysema.

Auscultation: Early it is normal, harsh vesicular breathing (will occur later).

± Adventitious Sounds

Rhonchi due to secretions or super imposed bronchospasm

Coarse non consonating crepitations due to secretions

Complications of chronic. Bronchitis / emphysema (COPD).

- Respiratory failure
- Secondary polycythaemia
- Rt. V failure
- Peptic ulcer
- Pulmonary hypertension with cor pulmonale
- Bronchiectasis
- Bronchial Carcinoma
- Nocturnal hypoxia.

*** Dyspnea occur in cases of COPD when FEV1 falls below 40% of predicted, hypercapnea occurs when FEV_1 falls below 25% of predicted.**

Pulmonary hypertension (P++) will developed in cases of COPD due to vasoconstriction of pulmonary arterioles and vasodilatation of peripheral arterioles with increase of blood flow to the lung leading to cor pulmonale. Also hypoxia causes polycythaemia with increased blood viscosity aggrevating cor pulmonale compression of the capillaries by the increased intra alveolar pressure also leads to P++

Investigations:

1. **X-ray** ↑↑ Bronchovascular markings
   Signs of emphysema (late).
2. **ECG** → Rt. v++, right axis deviation (cor-pulmonale)

3. Blood gasses → (↓ O_2 - ↑ CO_2) with type II respiratory failure.
4. Respiratory function tests → reveal ventilation defect (obstructive hypoventilation) see later.

Treatment

☆ Expectorants + mucolytics for sputum mobilization and bronchial drainage.

☆ Bronchodilators, inhaled B2 agonists can be used for patient with mild disease, ipratropium bromide bromide may be added for patients with moderate disease, oral B2 agonists can be added with severe disease. These drugs do not influence longevity in patients with COPD but can reduce symptoms. Aminophylline also can be used. These agents can be used separatelly or in combination.

☆ Steroids therapy (controversy), it is used in cases with severe bronchospasm resistant to bronchodilators.

We can give prednisolone 30 mg/d for 2 weeks as a trial, if there is improvement of respiratory functions (FEV1 increase >15%), tapering of steroids should be done with replacement by inhaled steroids to avoid the side effects of systemic steroids. The role of long term therapy with steroids is uncertain, but they may reduce the severity of exacerbations, however they do not slow the progression of disease.

☆ Avoid irritation, antibiotic during episodes of infection usually by , H-influenza or pneumococci, give amoxacilline 500mg/6hrs. Influenza and pneumococcal vaccines should be used, (long term antibiotic therapy is controversial).

☆ Long term domiciliary O_2 therapy has been shown to reduce symptoms and improve survival in chronically hypoxemic patients.

☆ Lung transplantation can be done for patients with severe COPD with FEV1 < 25% despite maximal therapy, particulary if associated with hypoxia and cor pulmonale.

☆ Resection of large localized bullae (bullectomy).

Treatment of acute exacerbation of chronic bronchitis

• Antibiotics • Bronchodilators • Diuretic therapy • O2 therapy
• Respiratory stimulant • Systemic or inhaled steroids. • Mechanical ventilation

Prognosis of chronic bronchitis

It is usually chronic progressive disease with exacerbations and eventually causing respiratory failure and right side heart failure.

Q Classification of COPD according to severity:

- Mild (FEV_1 60 – 70%), smoker's cough ± exertional dyspnea.
- Moderate (FEV_1 40-60%), exertional dyspnea ± wheeze, cough ± sputum.
- Severe (FEV_1 < 40%), dyspnea, wheeze and prominent cough + swollen legs.

II. Emphysema

Emphysema means pathologic accumulation of air in tissues or organs.

Types of Emphysema

1- Mediastinal emphysema or pneumo-mediastinum caused by rupture oesophagus (see later).
2- Subcutaneous emphysema due to chest wall injury or following surgery.
3- **Pulmonary emphysema**.

Pulmonary emphysema

Definition: Abnormal distention of air spaces distal to terminal bronchioles with destruction of the alveolar septa.

Causes:

1- **Emphysema associated with Chronic bronchitis** (COPD)
2- **Senile** → (atrophic emphysema). It is usually asymptomatic.
3- **Compensatory** → Bronchiectasis→emphysema of upper lung zone.
→ Unilateral lung disease→contralatral compensatory emphysema.

4- **Congenital**: Presented at middle age (ά1 antitrypsin deficiency).
Normally there are proteases (neutrophil elastase) which tend to digest the lung parenchyma (alveoli), So there are antiproteases, the most important of them is **α 1 antitrypsin**. So, in α1 antitrypsin deficiency the proteases will destroy the alveoli (protease antiprotease imbalance), cigarette smoking also accelerates the process.
5- Unilateral emphysema due to bronchiolitis **(Macleod's syndrome)**.

Pathology of pulmonary emphysema:

- Generalized distension and destruction of air spaces involves the whole of the acinus **(panacinar emphysema)** as in **α1** antitrypsin deficiency.
- In chronic bronchitis it is **(centriacinar)** affecting those alveoli and alveolar ducts closely related to respiratory bronchioles (COPD), while the more distal alveolar ducts and alveoli tend to be will preserved.
- Emphysema leads to expiratory airflow limitation and air trapping. The loss of lung elastic recoil results in an increase in total lung capacity, while loss of alveoli with emphysema results in decrease gas transfer.

Smoking → ↑↑ The number of the neutrophil in the lung leading to ↑ protease release → accelerates emphysema

C/P

Symptoms:

- Dyspnea, little or no cough except with chronic bronchitis.
- Symptoms of chronic bronchitis if present, as before (COPD).
- Symptoms of complications **e.g** :Respiratory failure, right sided heart failure and pneumothorax due to rupture of emphysematous bullae (chest pain).

O/E

General Examination: Congested neck veins with expiratory filling
Cyanosis with respiratory failure
Cor pulmonale.

Local examination:
- **Inspection** → ↓ movement , ↑ A- P diameter, symmetrical chest
- **Palpation** → Rt. V++, TVF ↓ or (equal on both sides)
- **Percussion** → Hyperresonance with encroachment on
  - The bare area of the heart
  - Hepatic dullness

  Also the Lower Border of the Lung is below 6th rib MCL
- **Auscultation** → Harsh vesicular breathing ± rhonchi, crepitations in cases of COPD (see chronic bronchitis)

Investigations

1- X-ray → Bronchovascular marking ↓↓, with hyperinflated lung.
Copulae of diaphragm are depressed, elongated heart.

2- ECG : Rt. V++ (cor pulmonale).

3- Blood gases → Respiratory FailureType **I** with pure emphysema (congenital).
Type **II** in emphysema with chronic bronchitis (COPD).

4- Assessment of the level of **α1** antitrypsin in serum.

Treatment:

1. No definite treatment, treatment of the cause and symptomatic treatment (see treatment of COPD).
4. In **α1** antitrypsin deficiency we can give α1 antitrypsin injection.

Q (Blue bloater, pink puffer) !?

Two classic types of COPD exist. Patients with dominant emphysema (Dyspneic) or type A COPD called **pink puffers**, but those with dominant bronchitic (tussive) or type B COPD called **blue bloaters**.

Pink Puffer (Type A fighter)

- This patient has dominant emphysema with mild hypoxia plus compensatory hyperventilation → (normal or mild decrease of arterial O_2 with hypocapnea)
- Puffer i.e. the patient try to keep the intra bronchial pressure above that within the surrounding alveoli so the patient expires the breath with pursed lips. This will prevent collapse of the bronchial wall which would result from the unopposed pressure of air trapped in the alveoli.
- It is usually occur with age > 60 years. There is progressive dyspnea and little or no cough and expectoration.

⇨ **Blue bloater** (Type B non fighter) (Bloater - Blue)
↓ ↓
Edema Cyanosis

- Patient with chronic bronchitis. + emphysema with dominant chronic bronchitis.

↓ ↓
Severe hypoxia Rt. V++ , right ventricular failure → edema
Leading to cyanosis and p++

- Blue blutter occurs at a relativelly young age with cough and expectoration plus wheezing.

Clinical abnormalities found in patients with advanced air flow obstruction (signs of severity of COPD)

- A reduction in the length of the trachea palpable above the sternal notch
- Tracheal descent during inspiration (**trachial tug**)
- Contraction of the sternomastoid and scalene muscles on inspiration
- Excavation of the suprasternal and supraclavicular fossae during inspiration.
- Jugular venous filling increased during expiration.
- Indrawing of the intercostal spaces during inspiration (**Littin sign**).
- An increase in the A-P diameter of the chest.

Q Chronic obstructive pulmonary disease i.e chronic bronchitis/emphysema:

- Aetiology of chronic bronchitis (as before).
- Pathology of chronic bronchitis with superimposed obstructive emphysema (centriacinar) as before.
- C/P of chronic bronchitis + S and S of emphysema (as before).
- Complications of COPD as before.
- Investigations of chronic bronchitis and emphysema as before.
- Treatment of chronic bronchitis and its complications.

Bronchial Asthma

Def. Bronchial asthma is an inflammatory disease of airways that is characterized by increased responsiveness of the tracheobronchial tree to a multiplicity of stimuli. It is pathologically characterized by a widespread narrowing of the air passages and clinically by paroxysmal attacks of dyspnea and wheezy chest which may be relieved spontaneously or as a result of therapy.

Causes and types: Etiologic or pathologic classification of the disease is difficult, however, asthma traditionally is divided into two forms.

Extrinsic asthma: **(**usually there is a definite external cause, mostly atopic**)**

Characterized by:

1- Early childhood (early onset asthma)
2- It occurs mostly in atopic individuals and usually with + ve. F.H. of atopy e.g urticaria or allergic rhinitis. It is usually seasonal !?
3- IgE ↑↑, so it is a classic type 1 IgE mediated hypersensitivity reaction to an inhaled antigen i.e (Immunologically mediated).

Ag + IgE → **mast cell** → release of mediators → bronchospasm

4- It is usually triggered by antigenic stimuli (allergens)
5- Prognosis → good due to (Natural desensitization!?)

Examples of antigens

1- Pollens, animal dander
2- Dust, Mites
3- Drugs e.g. penicillins, cephalosporines, sulfa
4- Food allergy.

Intrinsic: or cryptogenic (non atopic, the primary cause of increased airway reactivity is unkown !?)

Characterized by:

1- Starts in middle age (late onset)
2- -ve family history (for atopy)
3- No evidence of immediate hypersensitivity to specific Ag.
4- Ig A ↑↑ in some cases !?
5- It is usually triggered by respiratory tract infections, chemicals or drugs.

Pathogenesis of bronchial asthma (The inflmmatory process and its biochemical mediators)

1- Atopic (allergic or extrinsic asthma):

It is triggered by environmental antigens (dust, pollens, food ...) often with a positive F.H of atopy. It is a classic type 1 IgE mediated hypersensitivity reaction having:

- **Acute phase** with binding of Ag by IgE coated mast cells causing release of primary mediators (histamine, eosinophil and neutrophil chemotactic factors) and secondary mediators (leukotrienes, P.G, cytokines e.g IL4, IL5) these acute mediators result in bronchospasm, edema, mucus seccetion and recruitment of leukocytes.
- **A late phase** reaction (cellular phase) is mediated by recruited leukocytes (eosinophils, basophils, neutrophils) causing bronchospasm and edema with leukocytic infiltration.

2- Non atopic (non allergic or intrinsic asthma):

The mechanism of bronchial inflammation and hyperresponsiveness is much less clear in patients with intrinsic asthma.

It is often triggered by viral respiratory tract infections, chemical irritants and drugs with no evidence of IgE mediated hypersensitivity. The primary cause of increased airway reactivity is unknown. Some mediators e.g serotonin, prostaglandins and thromboxanes cause tissue inflammation and may particularly important in the pathogenesis of this type of asthma.

⇒ *Triggers of asthma or precipitating factors:*

1- The above antigens (1, 2, 3, 4).
2- Aspirin sensitive. Aspirin inhibits P.G synthesis→↑↑ production of leukotrienes from arachidonic acid, this is common in patients with allergic rhinitis with nasal polyps (this also occur with other NSAID).
3- Exercise induced asthma due to thermal changes within bronchial tree (Cooling and drying of bronchial mucosa)
4- Occupational asthma e.g. Byssinosis, spray painting, bakers, wood dust, varnishes and metal salt (Nickel).
5- Allergic bronchopulmonary aspergillosis → Aspergillus Ab in the serum of some patients.
6- Viral infection of respiratory tract e.g respiratory syncytial virus, rhinovirus or parainfluenza virus.
7- Stress induced asthma.
8- Cold air or dry air.

The tracheobronchial tree of asthmatic individuals appears to have an exaggerated reactivity (non specific bronchial hyperreactivity), to distinguish it from the bronchospasm provoked by immunologically specific antigens. The mechanisms underlying bronchial hyperreactivity are:

(1) **Muscle reactivity** i.e a change in the contractile mechanisms of airway smooth muscle.

(2) **Autonomic reactivity**:

(a) Parasympathetic system appears to mediate the reflex bronchial constriction.

(b) A deficiency in the sympathetic nervous system may be responsible for bronchial hyperactivity.

(c) The non adrenergic inhibitor system, it seems to inhibit bronchial constriction, deficiency of this system → bronchospasm.

(3) Inviromental factors e.g respiratory viral infections.

C/P

Sympt
- Episodic bouts of cough, dyspnea, chest tightness and expiratory wheezing usually provoked by exosure to allergens, emotional stress, viral infection and non specific precipitating events.
- Patients with episodic asthma are usually asymptomatic between exacerbations, this pattern of asthma is common in children or young adults who are atopic. In other patients the clinical pattern is of persistent asthma with chronic wheeze and breathlessness, this pattern is more common in older patients with adult onset asthma who are non-atopic and typifies intrinsic asthma.
- Acute severe asthma and its signs (see later).

O/E
- Harsh vesicular breathing + rhonchi + signs of hyperinflated chest. Rhonchi (generalized, mainly sibilant, mainly expiratory and persistent after cough), this is during the attack.

Cough variant asthma i.e recurrent attacks of bronchospasm presented with paroxysmal cough only with no dyspnea or wheezing.
Nocturnal cough may be the presenting symptom.

Complications of bronchial asthma

- Acute severe asthma
- Spontaneous pneumothorax
- Respiratory failure.
- Side effects of medications e.g arrhythmias.

Asthma per se does not cause emphysema or other chronic diseases, but it alone may be a significant cause of disability.

Investigations:

1- **X-ray** → there is no diagnostic features of asthma on the chest X ray but it may be helpful in excluding pneumothorax or pneumomediastinum as a complication.

2- **Blood gases** (during attacks)

☺ Mild cases → wash of Co2 due to hyperventilation → hypocapnea

☺ Severe cases → hypoventilation so Co2 either normal or elevated.

3- **Skin** hypersensitivity test for different antigens.

4- Blood
- ↑ Ig E with extrinsic asthma
- ↑ Ig A with intrinsic asthma !?
- Eosinophilia, leucocytosis.
- Positive aspergillus Ab.

5- Sputum smears may reveal:
* **Churschmann's spirals** = mucous that form a cast in the small airways.
* **Charcot leyden crystals** = breakdown products of eosinophils

6- Metacholine, histamine tests indicate the presence of non specific bronchial hyper-reactivity i.e bronchospasm at a lower dose in asthmatics.

7- Cold air challenge (i.e. inhalation of cold air → bronchospasm)

8- Challenge with specific agents in occupational asthma.

9- Respiratory function tests, FEV_1 is reduced but may improve after inhalation of bronchodilators.

Treatment of bronchial asthma

Goals of therapy:

(1) Maintain near-normal pulmonary function. (2) Maintain normal activity levels.
(3) Prevent recurrent exacerbations. (4) Avoid adverse effects of the used medications.

I. Treatment of bronchospasm during attack

Inhaled beta 2 – specific sympathomimetic

No response
↓
40-60 mg methyl prednisolone IV/6 hrs or hydrocortisone 200mg IV/6hrs
↓
No response
↓
Anticholinergic inhalers
Aminophyline IV injection

Good response
↓
Continue therapy, discharge, and arrange for follow up & treat as below (stepwise approach)

II. Stepwise approach to the therapy of bronchial asthma in between attacks

Some patients display only occasional attacks of exertional dyspnea and wheezing which respond to inhaled bronchodilators alone. Other patients have chronic symptoms requiring continuous use of inhaled or oral medications.

Step I → (Occasional symptoms less frequent than daily with PEFR i.e. peak expiratory flow rate 100%).

Occasional use of inhaled short acting B_2 agonist bronchodilators e.g. salbutamol (used as required). If it is needed more often than once daily or three times/week, shift to step II.

Step II → (Daily symptoms with PEFR ≤ 80).

Regular inhaled steroid (beclomethasone) 800 mcg/day plus inhaled short acting B_2 agonist as required. If there is unsatisfactory response, shift to step III.

Step III → (Severe symptoms with PEFR 50-80%).

High dose inhaled steroid 800-2000 mcg/day plus inhaled short acting B2 agonist as required. If no satisfactory response, shift to step IV.

Step IV → (Severe symptoms uncontrolled with high dose inhaled steroid with PEFR 50-80%).

As step III plus one or more of the following:

- Inhaled ipratropium bromide.
- Inhaled long acting B_2 agonist e.g. salmeterol 50 ug/12hr or formoterol 12 ug/12hr.
- Sustained release theophylline.
- Oral B_2 agonists.
- Leukotriene receptor antagonist (Montelukast sodium).

Step V → (Severe symptoms with deterioration with PEFR ≤ 50%) .

As step IV plus regular prednisolone oral in the lowest dose necessary to control symptoms in a single daily dose in the morning.

Severe symptoms with deterioration inspite of prednisolone therapy with PEFR ≤ 30%, hospital admission is required (step VI).

Pharmacology of drugs used in treatment of bronchial asthma

The pharmacologic agents for treating bronchial asthma can be divided into two general categories:

(1) Drugs that inhibit smooth muscle contraction i.e. bronchodilators (**quick relief medications**) e.g B2 agonists, aminophylline and anticholinergics.

(2) Drugs that prevent or reverse inflammation i.e. anti inflammatory (**long term control medications**) e.g corticosteroid, leukotriene inhibitors and mast cell stabilizers. These agents have a prophylactic or preventive actions.

I- Drugs used during attacks

A- B_2 agonist inhalers by metered dose inhaler **(MDI)**

Salbutamol (ventoline), terbutaline

= B2 agonist (bronchodilator)

Advantages ⇄ No side effects of systemic B2 agonist

Rapid action.

Dose: 2 puffs as required (100 ug/puff) for salbutamol and (250 ug/puff) for terbutaline

Use of MDI:

(1) The canister is shaken (2) The patient exhales the normal expiration.

(3) The aerosol nozzle is placed to the open mouth

(4) The patient simultaneously inhales rapidly and activates the aerosol.

(5) Inhalation is completed

(6) The breath is held for 10 seconds if possible.

B- Aminophylline I.V.

Dose: Loading dose: 5mg/kg (very slowly) then maintenance dose : 0.5 mg/kg/hr as in cases of acute severe asthma.

- Aminophylline is belong to methylxanthines
- In old age, heart disease or liver diseases→↓↓ dose of aminophylline
- In smokers or with phenytoin therapy → ↑↑ dose of aminophylline

C- Cortisone: → Hydrocortisone 200 mg/6hrs IV or methyl prednisolone 40-60 mg/6hrs IV.

Action: reduce airway obstruction

Anti - inflammatory Antiallergic

D- Anticholinergic: inhaler e.g ipratrobium bromide which is a non absorbable inhaler, it may enhance the bronchodilation achieved by sympathomimetics but is slow acting (60-90 minute to peak bronchodilation). The dose is 20-40ug three or four times daily.

E- Adrenaline: the patient must be (it is better to be avoided)

Not hypertensive Not cardiac

Dose: Solution (1/1000 – Amp), a dose of 0.3-0.5 mg.
i.e 0.3-0.5 ml. → S.C, it can be repeated after 20-30 minutes

II-Drugs used in between Attacks:

A- Aminophylline

The best is long acting preparation 100-200 mg/12 hr.
i.e Anhydrous Aminophylline , e.g (Quibron) tablets 300 mg.

Advantages: Less GIT irritation, long acting.

Mechanism: of action of aminophylline: It inhibits phosphodiasterase enzyme→↑ C-AMP → ↑ action of catecholamines.

B- Systemic B2 agonist: (bronchodilator)

* Salbutamol → Ventoline, Salbuvent
* Terbutaline → Bricanyl
* Dose 2-4 mg/d (oral)
* Side effects → Tremors, Tachycardia (palpitation)

C- Disodium cromoglicate [intal] Inhaler:
Stabilizes the membrane of mast cell → Decrease the release of mediators

D- Ketotifen: (zaditen), mast cell stabilizer.
Dose : 1 mg tab / 12 hrs

E- Leukotriene receptor antagonists e.g. montelukast (singulair 10 mg/d).

F- Cortisone:

a- **Local inhalers** :(Becotid) = Beclomethazone
Dose: 800ug up to 2000ug/d (200 or 250 ug per puff)
Side Effects: oropharyngeal candidiasis, To avoid we can wash the mouth by water after use.

b- **Systemic steroids**: (prednisolone)
Dose: 30- 40 mg/d → till improvement then low dose maintenance 5 - 10 mg/d. It is better to be substituted by inhaled steroid when possible.

G- Mucolytics and expectorants do not add significantly to the treatment of bronchial asthma.

H- Anti-IgE antibody therapy can be used in patients with high levels of IgE.

Acute severe asthma

Acute severe asthma (status asthmaticus) is a severe form of asthmatic attack not responding to the above classic therapy in 24 hours, it may persists for days or even weeks making the patient at risk of ventilatory failure.

Signs of severe asthmatic attacks, or acute severe asthma.

1- Tachycardia >110/m.
2- Exhaustion, patient can't speak in sentences.
3- Pulsus paradoxius.
4- Silent chest (No rhonchi)
5- Cyanosis.
6- Dehydration due to hyperventilation
7- Severe hypoxia – Normal or CO_2 retension.
8- Peak expiratory flow rate **(PEFR)** < 50% of the expected value by peak flow meter (patient asked to take a full inspiration and then blow out forcefully).

Treatment

(1) Hospitalization with full assessment including:

- Signs of severity of asthmatic attack, see later.
- Peak expiratory flow rate PEFR.
- Arterial blood gases.

(2) Initial treatment:

- O_2 with high concentration (60%), thereafter the O_2 concentration can be adjusted according to the arterial blood gases.
- Hydrocortisone 200 mg IV/4-6 hours for 24 hours then prednisolone 60 mg/day orally for 2 weeks then gradual tapering.
- Salbutamol by nebulizer (2.5-5 mg/4 hours) it can be repeated every 30 minutes as necessary, then 2.5 mg/4 hours once there is clinical response.

Then reassess clinically, PEFR, blood gases.

Satisfactory response

Reduce B_2 by nebulizer to 6- hourly then change the nebulised B_2 agonist to metered dose inhaler. Discharge patient with improvement and start the treatment in between attacks as before (stepwise approach).

Poor response

Add nebulised ipratropium bromide (500 ug)or aminophylline I.V or try B2 agonist I.V. If no mechanical ventilation → assisted ventilation.

Other measures in treatment of bronchial asthma

1. **Avoid Ag** if possible.
2. **Systemic desensitization**: by gradual S.C injection of small doses of Ag→to form Ig.G (blocking Ab) so when the antigen is introduced once more it well be attacked by Ig G and not by Ig E.
3. **Tryptizole** small dose 10-25 mg/d.
   It is a Tricyclic antidepressant → Sedative, Anticholinergic

Occupational asthma:
The affected persons are non atopic and the reaction usually occurs several hours after exposure.
Aetiology: Wood dust, animal dander, fungal Ag, platinum.
Diagnosis: History – Challenge test to demonstrate the cause.
Treatment: Avoidance + treatment as usual.

DD of bronchial asthma

- From other causes of paroxysmal dyspnea e.g cardiac asthma, tetany, myasthenia gravis and extrinsic allergic alveolitis.
- From other causes of paroxysmal dyspnea and wheezy chest e.g cardiac asthma, carcinoid $ and vasculitis e.g churg – strauss vasculitis.
- From other causes of paroxysmal cough e.g recurrent pulmonary embolism, whooping cough and extrinsic allergic alveolitis.

Brittle asthma (catastrophic sudden severe asthma)
It is an unusual variant of asthma in which patients are at risk from sudden death inspite of the fact that their asthma may be well controlled between attacks. Such patients require:

- Emergency medications at home, in the car and at work.
- Oxygen source at home and at work.
- Nebulized B_2 agonists at home and at work.
- Self injectable epinephrine at home, at work.
- Steroids.
- On developing wheeze, the patient should attend the nearest hospital, admission to intensive care may be required.

Q wheezy chest + haemoptysis

- Churg-strauss vasculitis
- Cardiac asthma (PVC)
- Allergic brochopulmonary aspergillosis
- Bronchiectasis

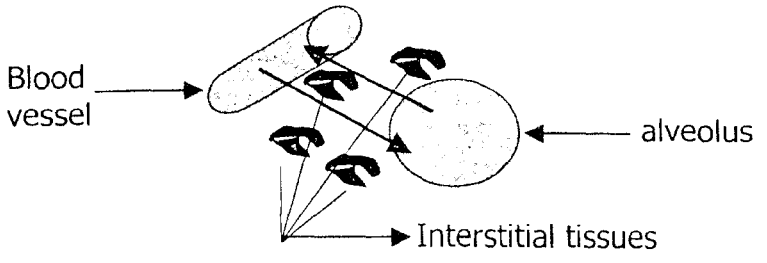
Respiratory Function Tests

Important definitions

- **Tidal Volume,** it is the volume of air in one breath during normal quiet breathing.
- **Residual Volume (RV)**, it is the volume of gas present within lung after a maximal expiration = 1200 ml.
- **Inspiratory reserve volume (IRV)**, it is the additional volume of air that can be inspired above the tidal volume = 3 L.
- **Expiratory reserve volume (ERV)**, it is the volume of air that can be forcefully expired after a normal expiration.
- **Vital capacity (VC)**, it is the volume of air expired after the maximal inspiration = 4600 ml.
- **Forced vital capacity (FVC)** is the same as VC, except that the inhalation is performed as rapidly and forcefully as possible.
- **Maximum breathing capacity** = volume of air expired after the deepest inspiration/minute.
- **Forced expiratory volume in 1 second (FEV_1):**
  The volume of air forcefully expired in the first second after a deep breath.
  - In the first second → most of vital capacity is expired, about 80% = FEV_1
    if ↓↓ = obstructive airway disease.
- **Total lung capacity (TLC)**, is the volume of gas in the lungs after a maximal inspiration, it equals the sum of the four lung volumes.

Pulmonary function tests for the following:

- **Ventilation**: How air moves in & out of the alveoli.
- **Perfusion**: Blood flow through the lungs and its distribution.
- **Diffusion**: Diffusion of O_2 and CO_2 between blood capillaries and alveoli.



I. Ventilation tests

Pulmonary causes of hypoventilation:

- **Restrictive**
  - Pulmonary fibrosis and interstitial lung disease
  - Pleural effusion
  - Pneumothorax
- **Obstructive**
  - Chronic bronchitis/emphysema (COPD)
  - Bronchial asthma.
  - Asthmatic bronchitis
  - Bronchiectasis and cystic fibrosis

Extrapulmonary causes of restrictive hypoventilation:

(I) Chest wall causes:

- Kyphoscoliosis
- Morbid obesity
- Ankylosing spondylitis

(II) Neurological causes of hypoventilation

- Myasthenia gravis
- Guillain Barre $
- Myopathy
- R.C. depression

Obstructive hypoventilation tests	Restrictive hypoventilation tests
• Vital capacity ↓	Marked ↓ of vital capacity.
• FEV1 marked ↓	FEV_1 Normal or increased relatively
• Residual volume ↑	Residual volume ↓

The hallmark of obstructive pattern is decrease in FEV1, but in restrictive pattern the hall mark is decrease in TLC and VC.

II Perfusion Tests

Pulmonary angiography — Perfusion scan (see C.V.S)

III. Diffusion tests

The diffusion is tested by arterial blood sample for blood gases, CO_2 is more diffusable, so diffusion defect leading to ↓ O2 with normal CO_2.

Respiratory Failure

Definition: It is a decline in the respiratory performance leading to hypoxia ± hypercapnea with the following arterial blood gases:

Po2 < 60 mmHg (normally it is 83-98 mm Hg)
± Pco2 > 55 mmHg (normally it is 36-45 mmHg)

Provided with normal atmospheric O_2 tension and absence of A- V shunts.
So respiratory failure is mainly a laboratory diagnosis.

Types:

Type I: Hypoxic normocapnic or hypocapnic as CO_2 may be washed due to hyperventilation, it is mainly diffusion defect.

Causes:

Acute

Acute pulmonary edema - ARDS
Pneumonia
Pulmonary embolism.

Chronic

Pure emphysema
Interstitial Pulmonary fibrosis-Lymphangitis carcinomatosa.

Type II: Hypoxic hypercapnic

It is mainly due to ventilation defect so → ↓ O_2 and CO_2 ↑

Causes:

Acute

- Respiratory muscle paralysis (see neurological causes of hypoventilation)
- Acute severe asthma.

Chronic

- Obstructive hypoventilation. e.g. COPD
- Restrictive hypoventilation e.g. pulmonary fibrosis and kyphoscoliosis.

Patient with chronic bronchitis + emphysema will suffer from ventilation +diffusion defect + perfusion defect → O2 ↓+ ↑ Co2 (type II respiratory failure).

C/P

(1) Features of hypoxia.

- **Acute** → Central cyanosis, tachypnea, tachycardia, convulsions and impaired consciousness.
- **Chronic** → Central cyanosis, clubbing, P++, cor pulmonale, polycythaemia, fatigue and drowziness.

(2) Features of hypercapnea.

Acute → Confusion then coma,

Chronic → Headache, drowsiness, hypersomnia (CO2 narcosis), flabbing tremors, ↑ ICT with papilloedema.

(2) Features of the cause.

Treatment of respiratory failure:

1- Treatment of the cause and the precipitating factor e.g antibiotics, bronchodilators, steroids.

2- O_2 therapy according to the type

Type I

There is O_2 ↓ with no ↑ CO_2

i.e CO_2 retention is not a risk.

- So we can give O_2 with high concentration
- Treatment of the cause
- Mechanical ventilation

  If necessary in acute cases and controlled long term O_2 therapy in chronic cases.

Type II

There is O_2 ↓ + ↑ CO_2, So ↑ CO_2→ ↓ sensitivity of respiratory center to Co2, So hypoxia → stimulate peripheral chemoreceptors → stimulation of breathing (**Hypoxic drive**) so correction of hypoxia → depression of respiratory center

- So in ttt of type II give low flow O_2 to preserve the hypoxic drive.
- Mechanical ventilation if necessary in acute or chronic cases.
- Also we can use doxapram as a respiratory stimulant.
- Controlled long term O_2 therapy in chronic cases.

Causes of acute exacerbation on top of chronic type II respiratory failure or causes of exacerbation of COPD

- Chest infection.
- Bronchospasm.
- Pneumothorax
- Pulmonary embolism.
- Retention of secretions .
- Heart failure.
- C.N.S depression.

Q: Disorders of ventilation

- Hyperventilation syndrome (see later).
- Hypoventilation (see before).

Hyperventilation syndrome: Means inappropriate over breathing (increase of the rate and or the depth of breathing) with washout of CO_2 leading to hypocapnea, $PCO_2 <$ 37 mmHg. It may lead to alkalosis if prolonged.

Causes:

(1) **Hypoxia**: • **High altitude**

(2) **Pulmonary disorders**: • Pneumonia • Pulmonary embolism • Bronchial asthma

(3) **Cardiovascular disorders**: • Heart failure • Hypotension

(4) **Metabolic disorders**: • Metabolic acidosis • Hepatic failure

(5) **Neurologic disorders**: • Psychogenic • CNS infections or tumours

(6) **Drug-induced**: • Salicylates • Aminophyline • B_2 agonists • Progesterone

(7) **Miscellaneous**: Fever – pain – pregnancy.

C/P:

- Neurologic symptoms may be present e.g. dizziness, visual impairment, syncope and seizure (secondary to cerebral vasoconstriction).
- Parasthesias, carpopedal spasm and tetany (secondary to decreased ionized Ca)

The disorders that frequently give rise to unexplained hyperventilation are recurrent pulmonary thromboembolism and anxiety hyperventilation.

Investigations: For the cause and blood gases for hypocapnea.

Treatment: Reassurance, treatment of the cause. Inhalation of a low CO_2 concentration e.g the patient is asked to breathe into a closed paper bag.

Although hyperventilation is frequently associated with dyspnea, patients who are hyperventilating do not necessarily complain of shortness of breath, and conversely, patients with dyspnea need not to be hyperventilating.

Pleural Diseases

Lung parenchyma is not sensitive to pain

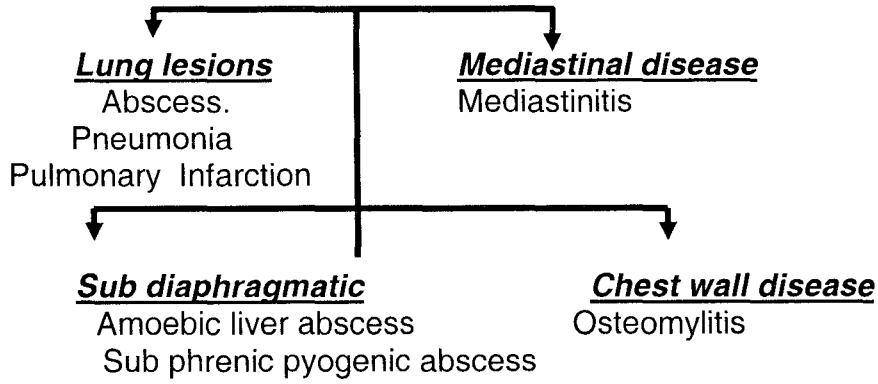
The sensitive structures are: • Parietal pleura • Bronchial & tracheal mucosa

Pain due to pleurisy of the central part of diaphragmatic pleura is reffered to the shoulder through phrenic nerve, while pain due to pleurisy of the outer part of diaphragmatic pleura is reffered to the upper abdomen through the lower intercostal nerves.

Acute dry pleurisy

Causes

1- Primary: viral, T.B., malignancy.
2- Secondary: to systemic disease as S.L.E., FMF, Rheumatoid disease
3- Extension from near by structures



C/P

(Pleurisy is not a diagnosis but simply the term used to describe an underlying disease)

1- Chest pain: • stitching • localized • increase with cough & inspiration
2- False dyspnea due to pleuritic pain
3- Diminished chest expansion in the affected side, palpable pleural rub may be present (pleural fremitus).
3- Pleural rub or pleuropericardial rub by auscultation.

DD of pleurisy

- Other causes of acute chest pain
- Differentiation between causes of pleurisy

Investigations: Directed to the cause e.g.:

- Plain X ray for pneumonia
- Lung scan for pulmonary infarction
- Markers for SLE, rheumatoid disease.

Treatment

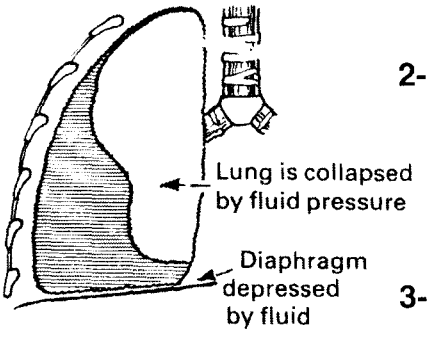
✪ NSAID for pain.
✪ Specific treatment for the cause.

Pleural Effusion

Definition: It is an abnormal accumulation of fluid in the pleural space.

- In healthy persons, the pleural cavity contains a small volume of lubricating serous fluid formed by transudation from the parietal pleura and absorbed by the capillaries and lymphatics. The balance between formation and removal of this fluid may be compromised by any disorder that increases the pulmonary or systemic venous pressure, lowers the plasma oncotic pressure, increases capillary permeability or obstructs the lymphatic circulation.
- A pleural effusion may be transudate that caused by elevated venous pressure or by decreased plasma oncotic pressure, it may be exudate that caused by increased permeability at the pleural surface (due to inflammation, trauma or lung disease) or by obstruction of lymphatics.

Aetiology



1- Transudate
- * Heart failure
- * Nephrotic $
- * Liver cirrhosis
- * SVC obstruction
- * Myxedema

2- Exudate →
- Lung disease **e.g** TB-Pneumonia - Malignancy
- Connective tissue disease e.g SLE.
- Sub diaphragmatic abscess
- Pulmonary infarction
- Uremia – pancreatitis (left sided effusion)
- Myxedema.

3- Hemorrhagic
- * Tuberculosis
- * Malignancy e.g bronchogenic carcinoma, mesothelioma.

4- Bloody ⟶ Haemothorax in chest injuries

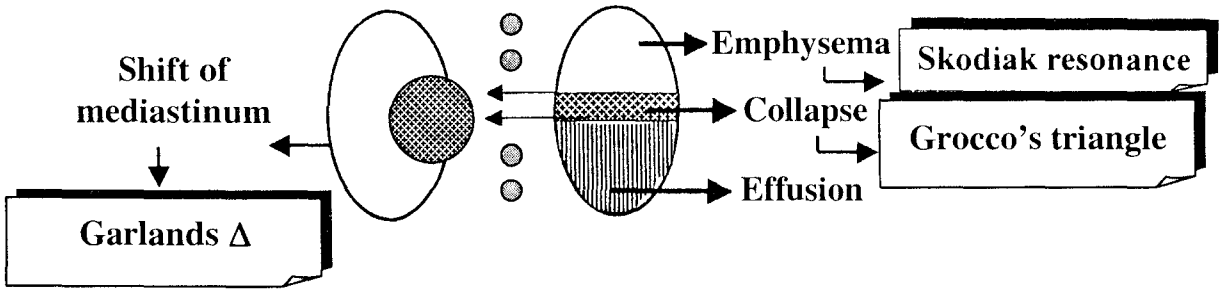
5- Chylous → Obstruction of thoracic duct by tumour, filariasis.

C/P

Symptoms
- Manifestations of the cause.
- Cough
- Dyspnea if the effusion fluid compresses the lung and interferes with the movement of the diaphragm.
- Dull aching pain, stitching pain if there is active inflammation.

Signs (Multiple negative signs)
- **1-** Inspection → Diminished movement, absent Littin sign.
- **2-** Palpation ⟶ Trachea shifted to the opposite side
  ↓ TVF
- **3-** Percussion → Stony dullness (basal and rising to the axilla!?, this may be only observed radiologically).
- **4-** Auscultation → Diminished intensity of breath sounds. Egophony is heard over the adjacent compressd lung.

Percussion in pleural effusion:
* **Skodiac hyperresonance** in upper part of lung above the effusion due to compensatory emphysema.
* Dullness just above the level of effusion due to lung collapse (**Grocco's triangle**).
* Dullness on the opposite side of effusion (**Garland's triangle**) due to shift of the mediastinum.



Investigations

1. **X-ray chest**: Homogenous opacity with obliteration of costophrenic angle, rising to axilla.
2. **P-A film may** show no abnormality if there is less than 300 ml pleural fluid. A lateral decubitus film may help to differentiate free fluid from previous inflammatory adhesions.
3. **Pleural biopsy** for → Malignancy
   → T .B.
4. **Aspiration** (Thoracentesis) → Transudate
   → Exudate:
5. **Diagnostic ultrasound** can localize the effusion more accurately.

N.B.: When ordinary measures fail to establish a definitive diagnosis and needle biopsy of the pleura is negative, thoracotomy or the recent technique of video assisted thoracoscopy (**VATS**) with exploration of the lung and biopsy of the involved areas of the pleura.

(Exudate)	(Transudate)
• Protein > 3gm/dL	• Protein < 3gm/dL
• Specific gravity> 1018	• Specific gravity < 101g
• Cells ↑↑	• Cell ↓↓ (WBCs)
• LDH > 200 IU/L	• No increase of LDH
• Low glucose level	• Glucose level is almost as blood

Other findings in pleural effusion fluid

1- ↓↓ Glucose → TB or tumour (low) - Rheumatoid disease (very low)
2- ↑↑ Amylase → Pancreatitis (It is typically left sided pleural effusion)
3- C3, C4 ↓↓ e.g. SLE
4- R.B.Cs ↑↑ Malignancy, T.B
5- LDH → ↑↑ with exudate. (> 250 mg/dl).
6- Malignant Cells → Malignancy
7- Z.N. or PCR for T.B.
8- PH < 7.2 with empyema.
9- Chylous effusion (milky white, rich in fat, clears on addition of ether and stained orange with sudan III.
10- Pleural fluid: serum protein ratio > 0.5 with exudates.
11- Pleural fluid: serum LDH ratio > 0.6 with exudates.

Treatment of pleural effusion

1- Treatment of the cause
2- Aspiration (Thoracentesis):

- **Diagnostic**
  - As above
- **Therapeutic**
  - To ↓↓ dyspnea
  - To ↓↓ incidence of fibrosis especially in T.B.

Complications of aspiration are haemothorax, hydropneumothorax and unilateral pulmonary edema with rapid thoracentesis due to sudden expansion of a collapsed lung.

Empyema

Def. : It is an accumulation of pus in the pleural sac. The fluid usually is thick and has the appearance of frank pus. As previously stated pleural fluid with a pH of less than 7.2 strongly suggests an empyema.

Causes
- Lung → pneumonia, bronchopneumonia lung abscess.
- Subdiaphragmatic→ Subphrenic abscess.
- Mediastinal infection

C/P

Cause → lung abscess, pneumonia

Symptoms

General
Severe FAHM (Toxemia)

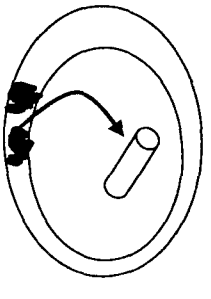
Local
- Cough
- Dyspnea
- Chest pain:
  - dull aching Pain
  - pleural stitching pain.

Signs: Toxic facies, fever

Local ex:
- **Inspection** → Diminished movement of the affected side
- **Palpation**
  - Mediastinal shift to the opposite side
  - TVF ↓ on the affected side
- **Percussion** → Stony dullness.
- **Auscultation** → ↓↓ intensity of breath sounds or diminished air entery

Complications

1- Pulmonary fibrosis
2- Bronchopleural fistula: Pus cells destroy the lung parenchyma → connection between pleura & bronchus so pus gets from pleural space to bronchus → cough with expectoration related to posture (cavitary lung $).



3- Amyloidosis kidney → Nephrotic $
4- Empyema necessitans → intercostals swelling giving expansile impulse on cough (it is necessary to be drained)
5- Septicaemia

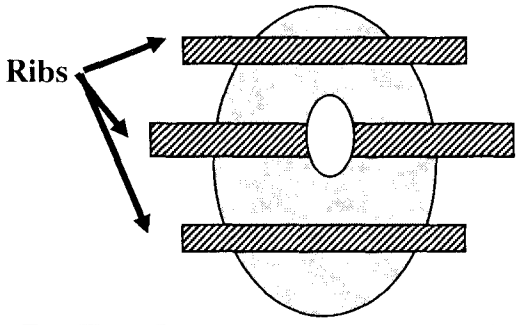
Investigations:

1- X-ray → opacity of effusion, encysted empyema may present.
2- Aspiration → culture & sensitivity.

Treatment of empyema:

1- Antibiotics with high doses according to culture and sensitivity.
2- Intercostal tube for free drainage.

If no response:



1- Antibiotics
2- Open drainage.

↓

Rib resection ± hole in the pleura with dissection of adhesions within the pleural cavity

3- Decortication:
= removal of pleura if open drainage is failed !?.

An empyema almost always requires chest tube drainage as well as antibiotic therapy. If the fluid itself is non infected with a relatively low WBC count and a pH of more than 7.2 the empyema may resolve with systemic antimicrobial therapy and tube drainage. However after several days without adequate drainage, most empyemas become loculated, so that tube drainage is not effective and rib resection is necessary to allow open drainage.

Pneumothorax

Def.: Presence of air in the pleural space, If the accumulating air is large enough, the underlying lung may become collapsed and functionless.

Etiological types:

(i) Spontaneous pneumothorax

- Rupture bleb (primary) subpleural emphysematous bullae.
- Severe asthmatic attack, rupture subpleural emphysematous bullae (secondary).
- Rupture of subpleural T.B cavity or lung abscess.

(ii) Traumatic pneumothorax

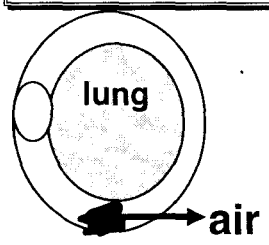
- Thoracentesis.
- Mechanical ventilation (ventilators).
- Penetrating chest injuries e.g. car accidents or stab wounds.

(iii) Artificial pneumothorax

- It was used in treatment of T.B (Collapse therapy) i.e. air is therapeutically introduced into the pleural space (not used now).

Pathological types (according to the intrapleural pressure):

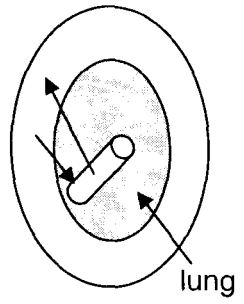
I-Closed Pneumothorax :



Air within pleura with no communication with the atmosphere

e.g. Rupture bleb → mild ↑ in pleural pressure, it is usually absorbed (regressive)

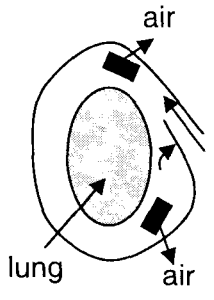
II- Open pneumothorax:



e.g. Trauma → bronchopleural fistula (air within pleura communicating with the atmosphere) so, with inspiration → air input into pleura → mild compression on the lung, during expiration, output of air from pleura to bronchus to the outside will occur.

So, there is mild compression on the lung

III-Tension pneumothorax = (valvular mechanism)



- It is a buildup of positive pressure within the pleural space, which rapidly produces severe respiratory embarrassment. Patients under going positive pressure mechanical ventilation are particularly at risk.
- Tension pneumothorax results from a ball-valve mechanism at the site of the airleak, which allows air to enter but not leave the pleural space e.g. due to trauma.
- This leads to progressive collapse of the lung, a contralateral shift of the mediastinal structures, and reduced blood flow to the right side of the heart, impairing cardiovascular function as well as lung function.

C/P Of Pneumothorax

Symptoms

1 Sudden onset of chest pain, the patient may feel that something ruptured e.g (rupture bleb or emphysematous bulla).
2 Anxiety (sense of impending death)
3 Severe dyspnea with severe cases, dry cough.
4 Shock, cyanosis and right sided heart failure with tension pneumothorax
5 Manifestations of the cause.

Signs

Mild → No signs (diagnosed by X ray)

Severe
- Inspection → Movement is diminished.
- Palpation → TVF ↓ , ↓ expansion, mediastinal shift to the opposite side.
- Percussion → Hyperresonance
- Auscultation → ↓↓ air entery (↓ intensity of breath sounds)
  → Amphoric breathing in open and tension types.
  → Pneumothorax click in left sided cases.

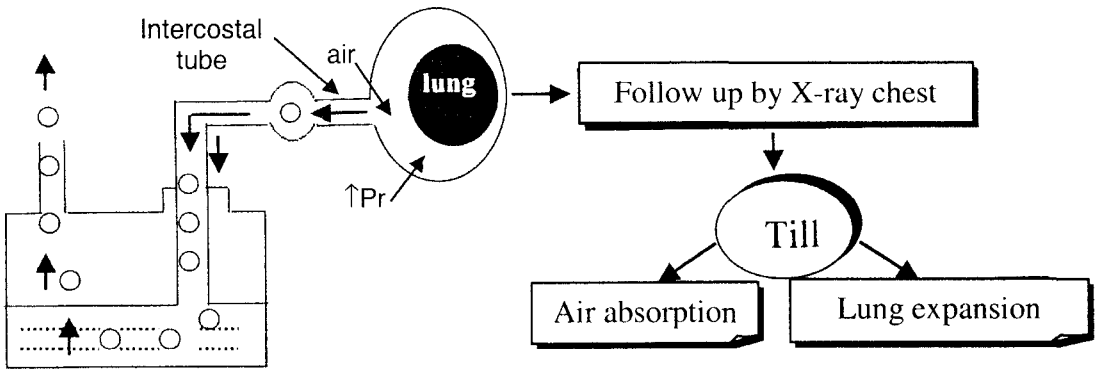
Q D.D.of chest pain + shock?
- Tension pneumothorax
- Massive pulmonary embolism
- Extensive myocardial infarction.
- Dissecting aortic aneurysm

Investigations:

1- **X-ray** chest, if obtained during expiration, may help to demonstrate small pneumothorax area because this technique increases the contrast between the lung and the pleural space.
2- Measurement of the intrapleural pressure by manometry.
3- CT scan chest.

Treatment

1- Cause.
2- A small spontaneous pneumothorax often resolves by itself.
3- Intercostal tube under H_2O seal for a more severe or a secondary pneumothorax for re-expansion of the lung.
This tube is inserted for 24-28 after the lung re-expansion.



In recurrent spontaneous pneumothorax (after 3 or more occurrences), pleurodesis can be done by intrapleural injection of glucose or tetracycline, this also can be used in malignant effusion resistant to treatment.

D.D of pneumothorax

- Causes of acute chest pain.
- Causes of acute dyspnea.
- Differentiations between the pathological causes of pneumothorax.
- Differentiations between the aetiological causes of pneumothorax.
- DD of tension pneumothorax (chest pain + shock).

Tension pneumothorax

Cause : Trauma-mechanical ventilation.

Path. : As before
: As before ± special symptoms & signs → Positive coin test, Marked dyspnea, Shock

Treatment: First aid → put a 16F cannula in the 2nd space MCL to change the tension to open pneumothorax then intercostal tube under water seal as before.

D.D → Chest pain + Shock (see before)

Pneumomediastinum

(Mediastinal emphysema,)

Air introduced within the mediastinum (see diseases of mediastinum)

Causes
- Rupture or perforation of trachea or oesophagus.
- Alveolar rupture with dissection of air into the mediastinum.

Diagnosis and treatment:

1- Chest pain without radiation.
2- Subcutaneous emphysema in the suprasternal notch may present.
3- Auscultation, Hamman's sign which is crunching or clicking noise synchronous with the heart beats, it is best heard in the left lateral decubitus.
4- It is confirmed by chest x ray.
5- In mild cases O_2 therapy → absorbition of air, severe cases need needle aspiration

Hydro and pyopneumothorax

Aetiology

(1) Introduction of air during aspiration of effusion or empyema.
(2) Empyema with broncho pleural fistula.
(3) Rupture of T.B cavity or lung abscess into pleura.

C/P

Symptoms:
- The cause, dyspnea, cough

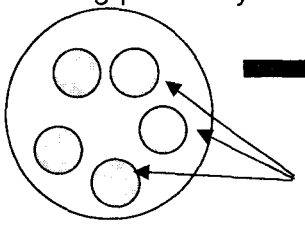
Signs
- **Inspection**: Diminished movement of the affected side.
- **Palpation**: TVF ↓, shift of trachea to the opposite side.
- **Percussion**: Basal dullness (not raising to axilla !?) with hyperresonance above, positive shifting dullness (see the clinical part).
- **Auscultation**: ↓↓ intensity of breath sounds, +ve succusion splash.

Investigations:
- X ray chest showing pleural effusion with horizontal upper level + jet black zone above (air).
- CT scan chest.

Treatment:
- Treatment of the cause.
- Intercostal tube can be used.
- Aspiration of (fluid and air)

Pneumonia

Def. It is an acute respiratory illness characterized by inflammatory reaction within the lung parenchyma (alveoli) → exudation into alveoli with consolidation.



Consolidation i.e. alveoli out of function

Alveoli full of exudates, so pneumonia considered to be an inflammatory consolidation

Predisposing factors:

1) Pneumococcal pneumonia often, Follows influenza or paranainfluenza Infection
2) Cigarette smoking
3) Alcohol excess
4) IV drug abuse (staph)
5) Immunosupression.
6) Aspiration with decreased conscious level
7) Hospitalized ill patient.
8) Bronchiactasis and COPD

It is helpful to consider pneumonia in two ways.

(a) Whether it developed at home (**community-acquired**) or in a hospital or institution (**hospital acquired**) or in **immunocompromised patient**.

(b) Whether it had a rapid onset with chills, fever and cough (**classical**) or a more gradual or indolent onset (**atypical**).

Classification of pneumonia:

1- **Community acquired pneumonia (CAP)**
   a. Pneumococcal (the commonest)
   b. Staphylococci, legionella, mycoplasma (common)
   c. Streptococci pseudomonas, klebsiella, H. Influenza (uncommon)
   d. Chlamydia, viral e.g. influenza and parainfluenza.

2- **Nosocomial pneumonia.**

3- **Pneumonia in Immunocompromised patient**.

Pathologically pneumonia can be classified according to the site of involvement of the lung into:

(a) **Lobar pneumonia** in which there is involvement of a large portion of or an entire lobe of lung. Pathological stages of lobar pneumonia are:
- Congestion with minimal exudation.
- Red hepatization with severe congestion, with alveoli full of RBCs and WBCs.
- Grey hepatization with alveoli full of leucocytes, fibrin.
- Resolution.

(b) **Bronchopneumonia**.

It starts as infection of bronchi and bronchioles which is aspirated into the alveoli and result in wide spread patches of consolidation, it is usually occur in lower lobes.

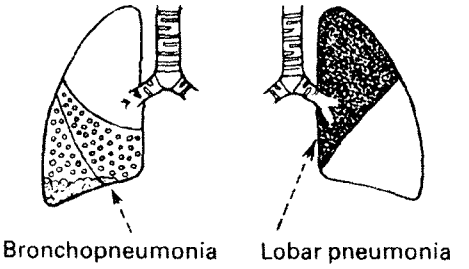
Lobar pneumonia can be caused by pneumococci (the main causative organism), klebsiella, staphylococci, streptococci or influenza. **Bronchopneumonia** caused by staphylococci, H influenza, streptococci.

(A) Community acquired pneumonia

Infection is usually spread by droplet inhalation and while most patients affected are previously well, cigarette smoke, alcohol and corticosteroids therapy, all impair ciliary and immune function are risk factors, other risk factors include old age, recent influenza or pre existing lung disease e.g. COPD.

C/P

symptom
- FAHM (toxaemia)
- Dyspnea
- Chest pain (pleurisy)
- Cough & expectoration of mucopurulant, rusty or blood stained sputum.



O/E
- **Inspection** → • Diminished movement, symmetrical chest.
- **Palpation** • Mediastinum is central , TVF ↑↑
- **Percussion** → Dullness
- **Auscultation** → Crepitations • Early → fine crepitation
  • Late→coarse consonating crepitations
  - Bronchophony
  - Whispering pectoriloquy.
  - Bronchial breathing

The previous signs in cases of lobar pneumonia usually are limited to one lobe of the lung, but the signs are usually bilateral and patchy and usually in lower lobes in cases of bronchopneumonia.

Investigations:

1- X- ray: Homogenous opacity of a large portion of or an entire lobe of lung in case of lobar pneumonia or bilateral patchy, consolidation often affecting both lower lobes in case of bronchopneumonia.

2- Culture **&** Sensitivity for sputum.

3- Blood picture → TLC ↑, PNL ↑ (bacterial infection) . ESR ↑↑

4- Blood gases showing hypoxia.

5- Serology:
- Detection of pneumococcal antigen by counter immunoelectrophoresis of sputum, urine and serum (It is more accurate than sputum or blood cultures).
- Mycoplasma antibodies IgM and IgG.
- Legionella and chylamydia antibodies.
- Legionella antigen in urine.

Unresolving pneumonia

This means active pneumonia inspite of antibiotic therapy for 2 weeks or more:

Immune suppression	T.B.	Atypical pneumonia e.g legionella, mycoplasma	Resistant organism e.g staph (MRSA)	Underlying disease e.g bronchial carcinoma

Treatment:

- Generally, pneumonia is better treated with parentral antibiotics, then we start oral antibiotics when there is clinical improvement and when fever subsides. The duration of treatment is usually not less than 2 weeks !?.
- Oral cephalosporins should not be used in the management of pneumonia as they do not penetrate well into sputum or bronchial fluids and do not cover likey organisms.

1- Antibiotic therapy for pneumococcal and streptococcal pneumonia.

- Penicillin G injection. 1-2 gm/6hours I.V.
- Erythromycin 500 mg/ 6hrs or clarithromycin (klacid) 500 mg/12hour I.V or orally in patients allergic to penicillin.
- Ampicillin or Amoxcillin 0.5-1 mg / 6 hrs I.V or orally.

2- Expectorant → K iodides.

3- Chest pain → NSAID (for pleurisy)

Special Types of community acquired pneumonia with specific features according to the type of organism

Features of pneumonia as before with specific features as follow:

1- Staph Pneumonia

- Extensive cavitation.
- Haemoptysis

Treatment: - Flucloxacilline 1-2 gm/6 hrs I.V plus clarithromycin 500 mg/12 hour I.V.
- Oral therapy can be started when fever subsides.
- Treatment for at least 2 wks
- Vancomycin (vancocin) for MRSA 0.5-1 gm I.V/12 hour.

2- Klebsiella : Usually affecting the upper lobe (**Friedlander pneumonia**)

Q DD. of apical Lung lesions
- → Friedlander pneumonia
- → T.B
- → Bronchiactasis sicca hemorrhagica
- → Pancoast tumor

Treatment : Antibiotics for gm – ve (for 2wks) e.g. gentamycin plus ceftazidime (Fortum, third G cephalosporins) 1 gm/8hour I.V or ciprofloxacine 200 mg/12 hour I.V.

3- Atypical pneumonia (There is congestion of the alveolar wall without consolidation)

Viral	**Mycoplasma**	**Legionella**	**Chlamydia**
•Influenza virus •Respiratory syncytial virus.	•Usually affect one of the lower lobes or both.	(gm +ve coccobacilli) It starts as lobar then becomes multilobar.	**Pneumoniae**

Diagnosis Atypical pneumonia syndrome is characterized by:

- More gradual onset, dyspnea.
- Chest complaints e.g pleuritic pain, productive cough are less marked in atypical pneumonia than in classical pneumonia.

- Prominence of extra pulmonary symptoms e.g. headache, malaise, myalgia, sore throat, gastrointestinal symptoms.
- Minimal signs on physical examination e.g few scattered crepitations.
- Investigations: Blood picture, ESR, sputum examination, x ray and serology as before.

Treatment • Viral → antiviral

• Mycoplasma and legionella → Clarithromycin 500 mg/12 hr I.V or erythromycine 500 mg/6hr I.V plus rifampicin 600mg/12 hr. Also Legionnaires' disease (legionella pneumonia) responds to fluoroquinolones e.g levofloxacine (Tavanic).

• Chlamydia → erythromycine or tetracycline.

Legionella infection may lead to SIADH leading to hyponatremia.

4- Actinomycosis: (suppurative granuloma)

- Formerly included among the fungi, now it is considered as a bacteria (mouth commensal). It is gm +ve branching bacteria.
- Occurs in impaired local defense, there is pus with sulphur granules, treated with penicillin G 2-4 gm I.V /6hrs.

(B) Pneumonia in Immunocompromised patients.

Pulmonary infection is common in patients under immunosuppressive drugs and in those with diseases causing defects of cellular or humoral immunity.

Common causes of immune suppression

☆ **Neutropenia** :
* Cytotoxic drugs
* Agranulocytosis.
* Acute leukaemia.

☆ **T cell defect**: ± B cell defect
* Lymphoma
* Chronic lymphocytic leukaemia.
* Immuno suppressive drugs.
* HIV

☆ **Disturbed antibody production** :
* Chronic lymphocytic leukaemia
* Multiple myeloma.

Organisms (opportunistic)
- Fungal (Aspergillus fumigatus)
- C.M.V.
- T.B, mycobactrium avium
- Pneumocystis carinii, actinomycosis israeli.
- Other organisms e.g staph, strept or H. influenza.

Diagnosis (As before)

- Fever, cough, dyspnea.
- The onset of symptoms tends to be less rapid in patients with pneumocystis carinii and mycobarterial infection.
- Some patients who cannot produce sputum for examination can be induced to do so by inhalation of nebulised hypertonic saline.
- Chest x-ray showing lung infiltrates.
- Bronchoscopy, bronchoalveolar lavage fluid examination are helpful for diagnosis.
- Lung biopsy if necessary in certain cases e.g pneumocystis carinii.

Treatment

- It is based on the etiological diagnosis.
- We can start with a third generation cephalosporin or a quinolone plus antistaph antibiotic, or an antipseudomonas penicillin plus an aminoglycoside.
- This treatment is thereafter tailored according to the results of investigations.

Pneumocystis Carinii

- ♦ It is the most common opportunistic infection in patients with AIDS.
- ♦ It is a fungus found in the air.

C/P • Fever and dyspnea • Dry Cough • ARDS

- ♦ Cough and dyspnea can be present several days or weeks before the onset of systemic symptoms or even a chest X ray abnormality.

Investigations - **X-ray** → bilateral pulmonary infiltrates, nodules or cavities.
- Transbronchial lung biopsy

Treatment - co-trimoxazole I.V injection 120 mg/kg in divided doses, (100mg/kg Sulfamethyoxazole and 20mg/kg trimethoprim) for 21 days
- **I.V.** Pentamidine in resistant cases or in patients allergic to sulpha (4 mg/kg/d for 21 days).

(C) Nosocomial pneumonia

It is a hospital acquired pneumonia in a patient who has been admitted for more than 48 hours. The mortality is 30%.

Factors predisposing to nosocomial pneumonia

(1) Reduced host defences:

- Reduced immune defences (e.g corticosteroid treatment, DM, malignancy).
- Postoperative reduced cough reflex and disordered mucociliary clearance (anaesthetic agents).

(2) Aspiration of nasopharyngeal or gastric secretions:

- Reduced conscious level.
- Nasogastric intubation.
- Esophageal achalasia or severe gastro-esophageal reflux.

(3) Bacteria introduced into lower respiratory tract:

- Endotracheal intubation.
- Tracheostomy
- Infected ventilators, nebulisers, bronchoscopes.

(4) Bacteraemia:

- Abdominal sepsis.
- I.V cannula infection.

Organism: → Mostly Gm - ve → Klebsiella, Pseudomonas
→ Others, pneumococci — staph aureus (MRSA) – anaerobic arganisms

- There is high rate of colonization of the nasophorynx of hospital patients with Gm negative bacteria, together with the poor host defences and general inability of the severely ill or semiconscious patients to clear upper airway and respiratory tract secretions.
- Residence in the hospital predisposes patients to skin and mucosal colonization by microbial flora different from that found in ambulatory patients.
- Antimicrobials given to prevent or treat infection may predispose patients to colonization and subsequent infection by hospital flora.
- Failure to observe appropriate infection control measures may permit the dissemination of hospital flora.

C/P and investigations:

- The clinical features and investigations are very similar to community acquired pneumonia.
- In patients who develops acute bronchopneumonia there is initially symptoms of acute bronchitis followed by fever and dyspnea. Pleural pain is uncommon.
- Early, the signs are those of acute bronchitis followed by crepitations.
- There is neutrophil leucocytosis with mottled opacities in both lung fields mainly in lower lung zones.

Treatment:

- Third generation cephalosporin e.g (cefotaxime) plus an aminoglycoside e.g (gentamicin).
- Aspiration pneumonia treated by co-amoxiclav (augmentin) 1.2 gm/8 hrs plus metronidazole 500 mg/8 hrs.
- Physiotherapy, O_2 therapy, fluid support.

DD of pneumonia:

* Pulmonary infraction.
* Pulmonary T.B.
* Pulmonary edema
* Pulmonary eosinophilia
* Inflammatory conditions below diaphragm e.g. hepatic amaebiasis and subphrenic abscess.

Causes of recurrent pneumonia :

- Bronchial obstruction e.g bronchial adenoma or carcinoma.
- Chronic lung diseases e.g COPD, bronchiectasis and cystic lung
- Recurrent aspiration e.g in alcoholics, epileptics and severe gastro-esophageal reflux.
- Immunodeficiency.

Complications of pneumonia:

1- Post- pneumonic effusion
2- Synpneumonic effusion
3- Post pneumonic lung abscess.
4- Post pneumonic fibrosis
5- Meningoencephalitis.
6- Empyema.
7- Septic shock, multi organ failure
8- ARDs
9- Pericarditis, myocarditis

Lung abscess

Definition : A lung abscess is a localized area within the lung parenchyma that develops from an initial pneumonic stage. The centre of the infected area first becomes necrotic and purulent.

Aetiology : (The causative organisms are S. aureus or S. pyogenes organism)

1- **Primary** (aspiration or inhalation) usually it is right and basal, the causes are:

- Loss of Consciousness
- G. anesthesia
- Gastro-esophageal reflux
- Alcohol abuse
- During vomiting

2- Secondary to:

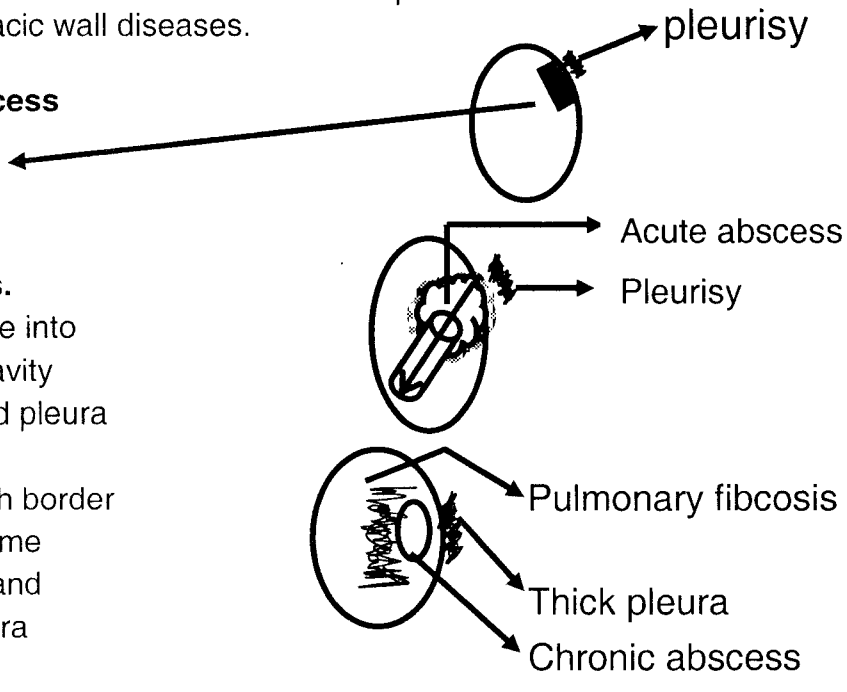
- ▶Lung disease ⇨ Pneumonia
  ⇨ Infected cyst
  ⇨ Bronchial carcinoma
- ▶Subdiaphragmatic → Amoebic abscess or subphrenic abscess.
- ▶Mediastinal & thoracic wall diseases.

Pathology of primary abscess

I. Pneumonic stage.
Area of consolidation
+ overlying acute pleurisy

II. Stage of acute abscess.
Suppuration & pus discharge into near by bronchus leaving cavity with irregular wall + inflamed pleura

III. Chronic abscess.
Cavity with regular & smooth border i.e the wall of abscess become intensely lined with fibrous and granulation tissue. The pleura becomes thick.



Lung abscess is usually is surrounded by pneumonic consolidation

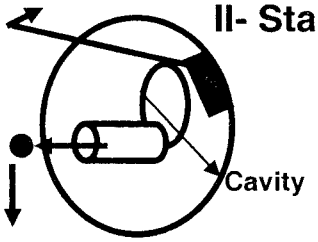
C/P:

I- Pneumonic stage

- FAHM
- Pleurisy → chest pain.
- Cough – dyspnea
- Signs of consolidation.

Diminished movement | ↑ TVF | Dullness | Bronchial breathing | Coarse consonating crepitations | Bronchophony whispering

Consolidation



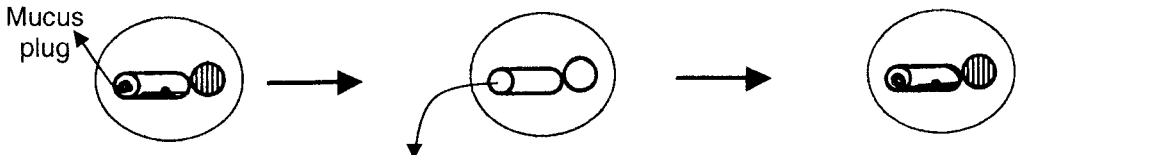
II- Stage of acute abscess (After about 1-2 weeks)

It is manifested with fever, toxaemia then the patient gets a severe attack of cough with expectoration of thick mucus plug followed by large foited sputum due to growth of anaerobes. This is usually followed by drop of fever **&** improvement of general condition.

Signs

- Diminished movement.
- TVF ↑ - Dullness
- Bronchial breathing – Bronchophony - whispering
- Coarse consonating crepitations.
- Post tussive suction (see the clinical part)

III- Stage of chronic abscess



Cavity full of pus → **Expectoration of mucous plug + evacuation of the cavity** → **Cavity full of pus again**

Symptoms:

* Toxemia (fever — anorexia – loss of weight-sweating)
* Symptoms of cavitary or suppurative lung with retension syndrome. (see DD)

Signs:

- General → Toxemia - clubbing of fingers
- Local → signs of cavity + fibrosis
  - Normal shape of the chest or retraction (fibrosis)
  - TVF ↑↑ (cavity), the mediastinum may be shifted to the same side (fibrosis)
  - Dullness
  - Bronchial breathing, bronchophony with coarse consonating crepitations (cavity).

Investigations:

- **X-ray** → cavity with fluid level
- Culture **&** Sensitivity. **(**for aerobes & anaerobes**)**
- **CT** scan chest
- Bronchoscopy is indicated when an abscess does not resolve completely with antibiotic therapy to exclude malignancy or foreign body.

DD of lung abscess (From other cavitary or suppurative lung $)

- **Lung abscess**
  - Acute onset
  - The expectoration ↑↑ on lying on healthy side
  - Retension **$** is common **(i.e.** attacks of cough with expectoration of large amount of sputum and evacuation of the cavity and then reaccumulation occurs .....)
- **Bronchiectasis**
  - Gradual onset
  - Long duration
  - It is bilateral, basal so the expectoration ↑↑ with leaning forward
- **Infected cystic lung** ⇨ see later
- **Empyema with bronchopleural fistula** diagnosed by **(**Methylene blue test**)** i.e. injection of methylene blue into pleural space → bluish colouration of the sputum.

Complications of lung abscess:

- Pneumonitis
- Bronchiectasis and fibrosis
- Pleurisy, pleural effusion and empyema.
- Amyloidosis e.g in kidney → Nephrotic $

Treatment: (The duration of antibiotic therapy is about 4-8 weeks).

1- Postural drainage

2- The antibiotic of choice is clindamycin (Dalacin-C) 600 mg/8hours I.V, then after clinical improvement and when fever subsides we give oral clindamycin 300-450 mg every 6 hours. Clindamycin must be combined with ampicillin or amoxicillin 2gm I.V/6hours then 500mg/6hours oral.

3- Metronidazole infusion then oral 500 mg/6hours can be used instead of clindamycin.

4- Ampicillin/sulbactam (unasyn) or amoxicilline/clavulanate (augmentin) are better to be used instead of ampicillin or amoxicilline.

5- Expectorants

6- Surgery for resistant cases e.g lobectomy or segmentectomy

Suppurative pneumonia is a term used to describe a form of pneumonic consolidation in which there is destruction of the lung parenchyma by the inflammatory process.
Although micro abscess formation is a characteristic histological feature, it is used to restrict the term pulmonary abscess to lesions in which there is large localized collection of pus.

Bronchiectasis

Def: It is pathologic irreversible dilatation of the bronchi and bronchioles caused by destruction of the bronchial wall, usually resulting from necrotizing suppurative infection of bronchi and bronchioles.

Aetiology & Pathogenesis

Obstruction (stasis with increase of the intrabronchial pressure) ⟷ **Infection** destroys the bronchial wall with increase of the bronchial secretions

↓

Dilated **&** suppurated bronchi and bronchioles

⇩

Bronchiactasis

Causes

I- Congenital

- Immotile cilia $ with stasis & infection
  - **e.g** Kartagner's syndrome ⇨
    - Bronchiactasis
    - Dextrocardia (situs inversus totalis)
    - Sinusitis or absent frontal air sinuses.
    - Infertility
- Congenital immune deficiency (recurrent infections)
- Congenital polycystic lung (see later)

II- Acquired

Obstruction

- **Complete**
  - Lung collapse !? with -ve pressure around bronchi and bronchioles.
  - ⇩
  - Traction on bronchi And bronchioles + infection
  - ⇩
  - Dilatation of bronchi and bronchioles
- **Partial**
  - **e.g.** Chronic bronchitis
  - ⇩
  - -Expiratory airway obstruction.
  - ⇩
  - Intra bronchial pressure With recurrent infections
  - ⇩
  - Dilatation of bronchi and bronchioles with suppuration.

Infection

- lung abscess or pneumonia
- ⇩
- This destroys the wall of the draining bronchi and bronchioles
- ⇩
- Dilatation & infection

T.B

- ⇩
- Bronchial stenosis
- ⇩
- Stasis with increase of the intrabronchial pressure with infection and dilatation of bronchi and bronchioles

→ **Bronchiectasis**

The small bronchi of childhood are most susceptible to bronchial infection and to obstruction by impacted secretions, foreign bodies or compressing lymph nodes. Seventy-five percent of patients can recall experiencing symptoms of bronchiectasis as early as the age of 5 years.

Chronic bronchitis is one of the commonest causes of bronchiactasis, this is due to partial obstruction and recurrent infections.

Sites **1- Bilateral & basal** (areas of poor drainage)

2- Apical on top of

T.B. — Friedlander pneumonia

This is called **bronchiectasis sicca haemorrgica (Haemoptysis + scanty sputum)**.

3- Right middle lobe $ (Brock's syndrome)

The right middle bronchus surrounded by lymph nodes

↓

Infections leading to lymph nodes enlargement

↓

Compression of the middle bronchus (obstruction with stasis)

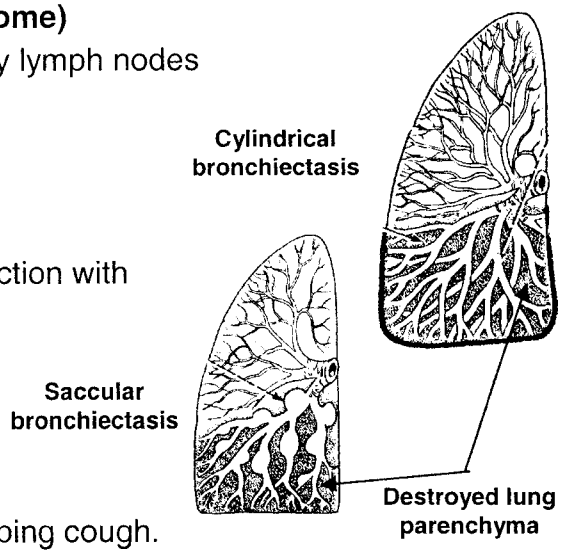
↓

Infection

↓

Bronchiectasis

This may be caused by T.B., measles or whooping cough.



C/P **Bronchiactasis is an obstructive and suppurative lung disease.**

Symptoms

1- FAHM

2- Cavitary$ → Sputum
→ Foited (bad odour)
→ Increased on stooping forwards

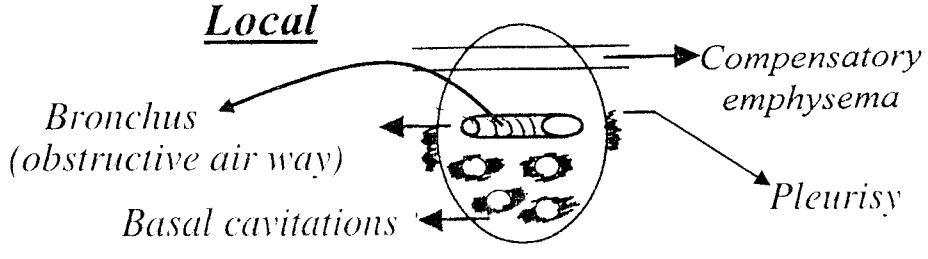
3- Haemoptysis (due to mucosal ulceration)

4- Dyspnea due to fibrosis and airway obstruction.

5- Chest pain due to: → Muscle Pain
→ Pleuritic Pain
→ Pneumothorax

Signs **General** → Toxemia
→ Clubbing – puffiness of eye lids (chronic cough)
→ Edema due to:

Cor Pulmonale — Hypoproteinemia — Amyloidosis kidney



- **Inspection** : Diminished movement, retraction with fibrosis (basal)
- **Palpation** :
  - TVF ↑↑ in lower lung zone (cavitation)
  - TVF ↓↓ in upper lung zone (compensatory emphysema)
  - Diminished chest expansion.
- **Percussion**:
  - Dullness in the lower lung zone (cavitation, fibrosis).
  - Hyperresonance in upper lung zone (compensatory emphysema)
- **Auscultation**:
  - Obstruction → Rhonchi, harsh vesicular breathing.
  - Secretions → Crepitations (coarse consonating crepitations)
  - Cavitation → Bronchial breathing + bronchophony and whispering.

Complications of bronchiectasis

General	Chest
• Haemoptysis	• Lung abscess
• Toxemia	• Pneumonia (aspiration)
• Amyloidosis	• Pleurisy. & empyema
• Septicemia	• Fibrosis
↓	• Cor Pulrnonale
Septic shock	

Investigations

1) Culture& Sensitivity
2) Plain x-ray → Honey comb appearance (basal)
3) Bronchography (old method), it is replaced by CT scan.
4) CT scan the best (can detect early bronchial dilatation) particularly high resolution CT scanning.
5) Pulmonary function tests may reveal either restrictive or a mixture of restrictive and obstructive ventilatory patterns.

Treatment

1) Postural drainage of sputum.
2) Antibiotic according to culture and sensitivity, flucloxacillin 500mg/6h for staph, ceftazidime 2 gm I.V/8hr or by inhalation 1gm/12hrs for pseudomonase, other antibiotics can be used e.g ciprofloxacine or inhaled to topramycin.
3) Expectorant &bronchodilator for bronchial drainage.
4) Surgery (lobectomy) for localized lesion causing:
  a. Persistent haemoptysis
  b. Persistent infection
5) Influenza and pneumococcal vaccines.

Bronchiectasis is rarely sufficiently localized for surgery, lung or heart lung transplantation is sometimes required.

Cystic fibrosis (mucoviscidosis) Or congenital polycystic lung

- There is a change in the viscosity and tenacity of mucous produced at apithelial surfaces.
- The disease includes mainly bronchopulmonary infection, pancreatic insufficiency and biliary cirrhosis with high sweat sodium and chloride levels.
- It is an autosomal recessive inherited disorder with gene mutation on the long arm of chromosome 7, producing abnormal membrane transport protein called cystic fibrosis transmembrane regulator (CFTR) leading to decreased chloride excretion into the airway lumen and increased reabrorption of sodium into the epithelial cells. So, less excretion of salt leads to less of secretion of water → increased viscosity of secreations.
- Also, there a CFTR independent mechanism of chloride secretion in the sweat glands with impaired reabsorption of sodium chloride in the distal end of the duct leading to increased salt content of sweat.

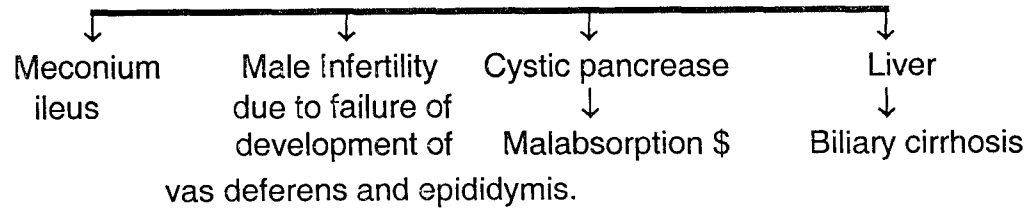
C/P

- The lung is the target organ of this systemic disease, it gives a picture similar to bronchiectasis plus extrapulmonary manifestations.
- Cystic fibrosis now is recognized as the most common cause of obstructive airway disease among individuals up to age 30 years. The median age of the disease has raisen from teens in 1960 to 30 years in 1998.

1- Pulmonary manifestations:

- The earliest pulmonary manifestation is peripheral airway obstruction due to plugged bronchi.
- Repeated bouts of infection lead to a cycle of obstruction and tissue damage. The predominant organism to colonize the lung is pseudomonas. Intial infections may be due to staph auteus.
- Many patients develop sinusitis and nasal polyps, clubbing of fingers.

2- (Extrapulmonary. Manifestations)



Investigations

- Chest X-ray → soap bubbles appearance
- CT scan chest
- Pancreatic functions
- NaCl in sweat is increased (the upper limit of normal sweat chloride concentration is 60 mEq/L)

Treatment

(A) **In early stages** of the disease, therapy must be individualized according to specific clinical manifestations:

(1) Salt depletion is a potential problem in warmer climates.

(2) Blocking of Na reabsorption with amiloride or stimulating chloride secretion with adenosine improves hydration of secretions.

(3) Nutritional supplementation and pancreatic enzyme replacement and vigorous treatment with parenteral antibiotics, hydration, humidification and supplemental oxygen.

(B) **In the late stages**, therapy is aimed at suppressing infections with antibiotics, post drainage and O_2 therapy. Dornase-α is a drug that makes sputum less viscid. Aerosolized tobramycin has demonstrated improved pulmonary functions!?.

(C) **In end stage disease**, bilateral lung or heart-lung transplantation is the procedure of choice.

Any pulmonary infection e.g (• **lung abscess** • **Bronchiectasis.** • **Pneumonia** • **Empyema**)

Leading to the following complications:

1- Systemic complications

- Toxemia
- Amyloidosis (except pneumonia)
- Septicemia
- Septic shock
- Meningitis

2- Local complications in the following structures:

Pleura ↓	**Parenchyma** ↓	**Bronchi** ↓
• Pleurisy	• Pneumonia	• Bronchiectasis
• Effusion	• Abscess	
• Emyema	• Fibrosis	
• Bronchopleural fistula		

3- Marked hypoxia e.g in cases of bronchiectasis leading to cor pulmonale.

Lung collapse

Aetiology

1- Congenital

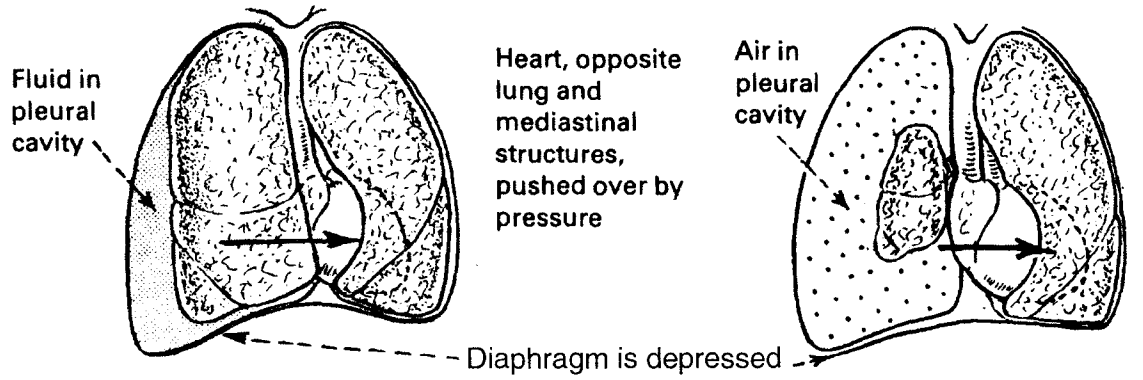
It is due to ↓ surfactant which is a lipoprotein secreted by the alveolar epithelium causing ↓ of the surface tension of fluids lining the alveoli.

Also, aspiration of amniotic fluid during labour → collapse

2-Acquired → Obstructive (absorption) collapse

- due to complete obstruction of bronchi
  - → Lumen : F.B., mucus
  - → Wall : Tumor or stricture
  - → Outside : LN or tumor

Compression Collapse → Due to pneumothorax or effusion


Fluid in pleural cavity
Heart, opposite lung and mediastinal structures, pushed over by pressure
Air in pleural cavity
Diaphragm is depressed

C/P

Symptoms

- Manifestation of the cause
- Dyspnea, cyanosis

Signs

Multiple negative signs

- **Inspection** → retraction, diminished movement ↓
- **Palpation**→ TVF↓ . TVF↑ if the underlying bronchus is patent.mediastinal shift to the same side
- **Percussion** → dullness
- **Auscultation** → ↓↓ intensity of breath sounds – bronchial breathing may be present if the underlying bronchus is patent.

D.D.

1- From other causes of $ of multiple -ve signs e.g effusion & fibrosis.

2- Consolidation

3- Acute dyspnea and post operative lung complications (see later).

Investigations

1- **X-ray** → Overcrowded ribs
→ Raised copula
→ Mediastinal shift → Homogenous opacity.
→ Collapsed lung → well defined border.

2- Bronchoscopy to detect the cause as F.B. or secretions and also to remove them

Treatment

a. Treatment of the cause
b. Bronchoscopy to remove F.B or secretions.
c. O_2 therapy
d. Breathing exercises.
e. Prophylactic antibiotics.

Postoperative lung collapse

Pathogenesis

1- Lack of pre-anaesthetic medications with bad preparation of patients.
2- General anaesthesia in presence of chest infection.
3- Neglected suction of chest secretions during and after operations.
4- Inability to cough properly after surgery in painful conditions.

Symptoms

Sudden onset of Postoperative

Dyspnea — **Cough** — **wheezy chest**

Signs

As above

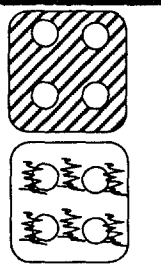
Treatment

- Prophylactic → see above.
- Active treatment:
  As above + postural drainage to remove the secretions

Q postoperative pulmonary Complications

1 -Aspiration Pneumonia
2-Aspiration lung abscess
3- Pulmonary embolism
4- Collapse
5-ARDS
- ↑↑O2 (toxicity)
- Sepsis

Pulmonary fibrosis



Types

- Interstitial pulmonary fibrosis (see later).
- **Parenchymatous pulmonary fibrosis:**

Etiology: TB – lung abscess – Bronchiectasis - Empyema

C/P

Pulmonary fibrosis (parenchymatous)

1- Manifestations of the cause or past history of → T.B, Abscess, Empyema., Bronchiectasis
2- Dyspnea, chronic dry cough
3- Cyanosis (In advanced stage)

Local examination (The affected side showing multiple negative signs):

- Inspection → Diminished movement, retraction.
- Palpation → TVF ↓, diminished chest expansion, trachea deviated to the same side of the lesion.

TVF↑ with marked tracheal shift to the same side

- Percussion → Dullness, if the fibrosis is left sided it does not affect the traube's area (resonant traube's area), to be differentiated from left sided pleural effusion.
- Auscultation → Air entery ↓↓ or ↓↓ intensity of breath sounds, coarse non consonating crepitations

Investigation

* **X-ray** → Crowded ribs, trachea shifted to the same side; Heterogenous opacity; Tenting of diaphragm
* **Pulmonary function tests** showing restrictive hypoventilation.

Treatment

- Treatment of the cause if possible.
- Symptomatic treatment e.g. antitussive for cough
- Treatment of complications e.g cor pulmonale and respiratory failure.
- Lung transplantation in advanced cases.

Bronchogenic Carcinoma

It is the most common malignancy in males, it accounts for 32% of all cancer deaths in men, 85% of patients die within 5 years.

Aetiology : and incidence (no definite aetiology)

- Male > female
- Peak incidence occurs between ages 55 and 65 years.
- Predisposing factors:
  - The major cause is tobacco use particularly cigarette smoking (3,4 benzpyrine) is the carcinogenic substance especially if combined with asbestos.
  - Air pollution (coal combustion, cadmium and radon).
  - Occupation inhaled substances e.g asbestos, nickel and arsenic.
  - Radiation e.g atomic bomb survivors, uranium miners.
  - Genetic mechanism e.g dominant oncogenes and loss of tumour suppressor genes.

Cigarette pack years of cigarette smoked indicating the degree of risk of developing bronchogenic carcinoma.

i.e. The risk is increased 40 times fold for man smoking two packs /d. for 20 years

Pathology

1- **Central or hilar** type in a main bronchus, it invades the mediastinum early
2- **Peripheral** in small bronchus, it invades pleura early
3- Pancoast tumour, it is apical and invades the thoracic inelt early.

- **Naked eye appearance** Fungating mass - Malignant ulcer - Infiltrative type
- **Microscopic**:

WHO classification

Type I	Type II	Type III	Type IV
• Squamous cell Carcinoma 35% Presents as Obstructive lesion → infection, it occasionaly cavitates	• Small cell car (oat cell car) 20% Highly malignant, responds to chemotherapy	• Adenocarcinoma 30% Associated with asbestos, invasion of pleura is common.	• Large cell 15% Early metastases.

Spread

- Direct → lung , pleura, mediastinum, brachial plexus, sympathetic chain and phrenic nerve.
- Lymphatic spread
  - Hilar & mediastinum, then cervical L.N.
  - Retrograde lymphatic → (lymphangitis carcinomatosa) → cor pulmonale
- Haematogenous → bones, liver, brain

Bronchoalveolar cell carcinoma (Bronchiolar carcinoma) arising in the terminal bronchioloalveolar regions accounts for 1-2% of lung tumors. It may be a peripheral solitary nodule or diffuse nodular lesion. It occurs in men and women equally and usually not associated with smoking.
It may be associated with expectoration of a large volumes of mucoid sputum.

C/P

A change in the character of the regular cough of a smoker old male, particularly if it is associated with other new respiratory symptoms, should raise the possibility of bronchogenic carcinoma.

I- Thoracic manifestations

A- Bronchopulmonary presentations:

1- Asymptomatic (detected accidentally by routine x-ray as coin shadow)

2- Cough and haemoptysis → Blood tinged sputum → Red current jelly
i.e. sputum consist of → → Tissue debris → Mucous → RBCs

3- Bronchial obstruction

Partial	**Complete**
• Emphysema	• Lung collapse
• Bronchiectasis	

4- Pneumonia usually recurrent at the same site, or is slow to respond to treatment.

5- Lung abscess (due to secondary infection)

6- Thoracic inlet syndrome may occur due to bronchial carcinoma in the apex of the lung (**superior sulcus tumour**) causing invasion of:

- ✪ Upper 3 ribs
- ✪ Sympathetic chain → (**Horner $**)
  - Ipsilateral partial ptosis.
  - Ipsilateral enophthalmos and a small pupil
  - Ipsilateral hypohidrosis of the face.
- ✪ SVC obstruction (congested non pulsating neck veins)
- ✪ Lower trunk of brachial plexus (**Pancoast's syndrome**).

• Pain in shoulder and inner aspect of the arm	• Wasting of the small muscles of the hand

- ✪ Subclavian artery → unequal pulse volume in both upper limbs

7- Cor pulmonale due to lymphangitis carcinomatosa.

B - Pleural presentations:

► **Effusion**:

- Malignant effusion (Exudate) → Massive, Hemorrhagic, Rapidly re-accumulating
- Transudate: due to obstruction of azygos vein
- Chylous: due to obstruction of the thoracic duct
- Empyema: due to rupture of malignant abscess into pleura

► **Dry pleurisy may occur**

C - Mediastinal presentations:

Mediastinal spread may result in dysphagia (see later, mediastinal syndrome)

2- Extra-thoracic manifestations

Metastatic

* Haematogenous spread

↓ ↓ ↓

Bone Liver Brain

↓

Pathological fractures

* Lymphatic spread
  - Cervical LN
  - Axillary LN
  - supraclavicular LN
  - Scalene L.N
  - Mediastinal LN

Non - metastatic

(Paramalignant $)

Due to production of abnormal metabolites by the tumor. This occurs commonly with small cell carcinoma, also this can occurs with other types.

- **Clubbing** with pulmonary osteoarthropathy
- **Neurological**
  - Myopathy
  - Neuropathy
  - Myasthenia gravis (**Eaton Lambert $**)
  - Cerebellar degeneration
- **Endocrinal**
  - Cushing $
  - Carcinoid $
  - Hypercalcaemia due to secretion of PTH related peptide.
  - ADH ↑ (SIADH) -
  - Gynaecomastia
- **Skin**
  - Pruritis
  - Herpes zoster
  - Dermatomyositis
  - **Acanthosis nigricans**
- **Haematological**
  - Thrombophlebitis migrans
  - Anemia – DIC.

- Hypercalcemia is usually caused by squamous cell carcinoma.
- Syndrome of inappropriate ADH and ectopic ACTH seretion are usually associated with small cell carcinoma.
- Clubbing most often with non small cell carcinoma.
- Gynecomastia is usually with large cell carcinoma.
- Hypertrophic pulmonary osteoarthropathy is usually with adenocarcinoma.
- Neurological syndromes may occur with any type of bronchial carcinoma.

Investigations

- X- ray
  - Coin shadow
  - Mediastinum mass
  - Effusion
  - Cavity, collapse.
  - Diaphragmatic paralysis
  - Rib erosion
- CT scan chest
- Sputum examination (cytology) for malignant cells, this may be helpful in patients who are not fit for bronchoscopy.
- Bronchoscopy → biopsy and bronchial brush samples, also it can assess the proximity of central tumours to the main carina.
- L. N biopsy from scalene pad of fat
- Mediastinoscopy (for local extension)
- Pleural biopsy in patients with pleural effusion.
- If bronchoscopy fails to obtain a cytological diagnosis, percutaneous needle biopsy under CT guidance may be helpful in patients with peripheral tumours.
- Laboratory investigations for paramaliganant $.

D.D • Lung abscess. • Pneumonia • T.B. • Pulmonary infarction
• Other causes of pleural effusion &mediastinal syndrome

Treatment:

I) Surgery:

* Surgical resection is the therapy of choice for patients with non small cell carcinoma who are operable candidates.
* (5-10% of cases are suitable for resection and about 70% survive for 5 years)

Criteria of operability:

- When the tumor is confined to the lung
- Away from carina by > 2 cm
- Good lung functions.
- No distant or localized spread

Pneumonectomy + irradiation.

II) Radiotherapy:

(A) Radiation therapy for cure:

* High dose radiotherapy can produce results that are as good as those of surgery in patients who have slowly growing squamous carcinoma.
* Radiation therapy is the treatment of choice if the tumour is inoperable, poor lung function is a relative contraindication.

(B) Symptomatic radiation treatment:

* It is used for bone pains and haemoptysis and also to decrease SVC obstruction.

III) Chemotherapy:

✪ **Small cell carcinoma (chemosensitive)**

* Combination of cisplatin and etoposide may increases the survival at 5 years from 15% to 25%, cranial radiation can be combined with chemotherapy, this particularly efficient at preventing brain metastasis, this is because small cell carcinoma frequently metastasizes to the brain.

✪ **Non small cell carcinoma**

* Trials of cisplatin based combination chemotherapy can improve the 5-years survival. Radiotherapy also can be combined with chemotherapy.

IV) Laser therapy, endobronchial irradiation and tracheobronchial stents:

(A) Lasser passed through a bronchoscope can be used to vaporize inoperable fungating intraluminal occluding carcinoma.

(B) Endobronchial irradiation (brachytherapy) for intraluminal tumour and malignant extrinsic compression.

(C) Tracheobronchial stents (made of silicone) for strictures caused by the tumour or from external compression.

Bronchial Adenoma

Def. Slowly growing intrabronchial lesions that represent 50% of all benign pulmonary neoplasm 80-90% are carcinoids, 10-15% are adenocystic and 2-3% are mucoepidermoid. Bronchial adenoma considered to be a locally malignant or a locally invasive tumour.

C/P (female = male)

1- Cough and recurrent haemoptysis (the tumour is highly vascular)

2- Bronchial obstruction with recurrent pulmonary infections, lung collapse may occur.

3- Carcinoid **$** attacks of → Bronchospasm, → Flushing, → Diarrhea

Investingations

- **X-ray** → Coin shadow
- Bronchoscopy → Biopsy (bleeding should be anticipated)
- **HIAA** → Hydroxy Indole Acetic Acid in urine
  = metabolite of serotonine

Treatment:

- Surgical Resection of the lobe or the segment that contain the tumour.
- Local removal of the tumour tissue from the bronchial lumen (bronchotomy with local excision), laser therapy may be needed.
- Chemotherapy, radiotherapy also can be used.

Mesothelioma

(1) Localized fibrous mesothelioma

This uncommon tumour arises from the pleural surface and most commonly is attached to the visceral pleura.

C/P

- Chest discomfort.
- Dyspnea.
- Hypertrophic pulmonary osteoarthropathy with arthralgia of the hands, ankles, wrists and knee plus clubbing of the fingers.

Investigations: chest x-ray showing mass ± pleural effusion.

Treatment: Surgical resection.

Prognosis: Most of these tumours are benign with good prognosis. A few of these tumours are malignant but have favorable courses.

(2) Diffuse malignant mesothelioma:

This tumour occurs with average age of 55 years. The incidence is increased with asbestos exposure, the malignancy develops 20 or more years after exposure.

C/P: Chest pain and dyspnea are the predominant symptoms.

Investigations: Chest x-ray showing pleural thickening or pleural effusion or both. Open pleural biopsy is often necessary.

Treatment: Radiation or chemotherapy with unsatisfactory results.

Patient with asbestos exposure with clubbing, DD:

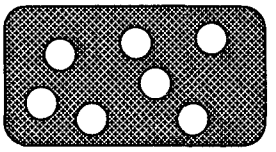
- Mesothelioma
- Bronchial carcinoma
- Interstitial pulmonary fibrosis

Interstitial pulmonary diseases And Interstitial Pulmonary fibrosis

Def. Group of chronic, non malignant, non infecious diseases characterized by inflammation and infiltration of the interstitial tissue of the lung with inflammatory cells with derangement of the alveolar walls and perivascular and perilymphatic tissues.

Pathological stages

(1) Acute stage:



There is acute damage to capillary and alveolar epithelial cells leading to interstitial edema. This stage may either resolve completely or progress to acute interstitial pneumonia.

(2) Chronic stage:

There is extensive deposition of collagen resulting in wide spread fibrosis. In addition there is disruption of the alveolar spaces, which are lined with atypical cuboidal cells.

(3) End stage:

The disease eventually progresses until the lung becomes honey combed. The entire alveolar and capillary network is replaced with fibrous tissue with dilated spaces. The capillary bed is decreased and the involved lung has no remaining gas exchange function.

Pathogenesis

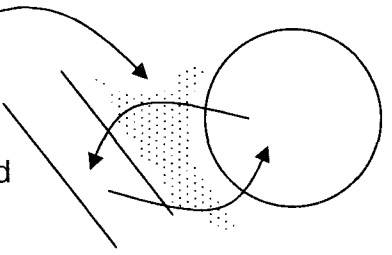
The causes of the interstitial pulmonary disease may lead to:

► Triggering of immune system?

Or ► Direct injury?

↓

Interstitial infiltration with inflammatory cells, with release of (platelet derived growth factor and transforming growth factor) and O_2 free radical



↓

Diffusion defect with hypoxia

↓ ↓

Recovery if the cause is avoided with early treatment

Interstitial pulmonary fibrosis (irreversible)

↓

Cor pulmonale and respiratory failure

Causes

1- **Dust** (occupational lung diseases)

- Inorganic dust (Pneumoconiosis)
- Organic dust (Hypersensitivity pneumonitis)

2- **Sarcoidosis**

3- **Collagen diseases**
- SLE
- Rheumatoid diseases.
- Scleroderma
- Ankylosing spondylitis.

4- **Idiopathic** (cryptogenic fibrosing alveolitis)

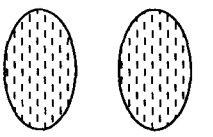
C/P

Features of interstitial pulmonary diseases:

1- Cause **e.g.** history of exposure, arthropathy.

2 Dyspnea + **5C**
- Cough (dry and irritative)
- Cyanosis
- Crepitations (fine with leathery character)
- Clubbing
- Cor pulmonale

Investigations



1. X-ray, diffuse lung infiltrates (miliary shadow) Or diffuse reticulo nodular pattern.
2. Blood gases showing diffusion defect ($\downarrow\downarrow O_2$)
3. CT scan especially high resolution CT.
4. Lung biopsy (open or transbronchial)
5. Examination of bronchoalveolar lavage fluid.
6. Pulmonary function tests showing diffusion defect (early) with super added restrictive hypoventilation (late).
7. LAB tests for the cause e.g ANA or Rheumatoid factor.

Treatment:

1) Avoid the cause
2) Antioxidants.
3) Bronchodilators.
4) Steroids (early with active disease).
5) Cytotoxic drugs can be used e.g. cyclohosphamide with steroid.
6) Pneumococal and influenza vaccines.
7) Oxygen therapy and treatment of right sided failure.
8) Lung transplantation.

Colchicine, penicillamine, interferon and cyclosporine have been tried, however their role remains to be determined.

- Corticosteroids are the mainstay of therapy and are indicated when lung biopsy show an active cellular process without extensive fibrosis. Large doses e.g prednisone 1 mg/kg/day may be used initially with physiologic and radiographic monitoring. It there is improvement after 6 weeks, the dosage should be tapered gradually with low dose maintenance if needed plus frequent monitoring to detect relapse.
- If no improvement with steroid alone, immunosuppressive agents may be used either alone or in combination with steroids. Azathioprine is the most widely used, cyclophosphamide and chlorambucil also have been used.

Separate types of interstitial pulmonary Diseases

1-Pneumoconiosis :

Occupational lung disease due to inhalation of inorganic dust

A- Asbestos related

- Interstitial Pulmonary disease (asbestosis) as above
- Pleural effusion (non malignant)
- Bronchogenic carcinoma
- Mesothelioma

B- Silicosis :

- Interstitial pulmonary disease (as above).
- T.B. may modify the silicotic process by enhancement of caseation and calcification. Also patients with silicosis are at higher risk for tuberculosis.

2- Extrinsic allergic alveolitis or hypersensitivity pneumonitis:

Extrinsic allergic alveolitis (e.g. farmer's lung) due to inhalation of actinomycetes present in the (hay).

C/P Symptoms usually developed 4-8 hours after exposure in sensitized patients and persist for few days.

- Cough
- Dyspnea
- Fever

- with repeated chronic exposures Interstitial pulmonary fibrosis will be developed late (as before).

Other selected example of hypersensitivity pneumonitis:

- Bird fancier's lung: Antigens from feathers or excreta.
- Bagassosis: Antigens from thermophilic actinomycetes in sugar cane residue.
- Humidifier (air conditioner) lung: Antigens from thermophilic actinomycetes in humidifiers or air conditioners.
- Mushroom worker's lung: Antigens from spores of thermophilic actinomycetes in compost.

Other occupational lung diseases

Coal workers pneumoconiosis

i.e inorganic dust, two types

↓ ↓

Simple pneumoconiosis

- It is a radiological finding
- It doesn't_progress to fibrosis

Interstitial pulmonary diseases as before

Byssinosis (cotton)

It is an obstructive airway disease due to inhalants.

☺ Initially → Bronchiolitis

☺ Chronic → occupational bronchial asthma

Q Humidifier fever

It is caused by water borne micro organism including amoeba from contaminated humidifiers in air conditioning systems.

C/P

Fever - dyspnea (bronchiolitis) → self limiting

N.B.: Legionella can be transmitted from humidifiers→ pneumonia

Q Obstructive airway disease due to inhalalants?

- Byssinosis
- Occupational asthma
- Industrial bronchitis e.g coal dust and gold mine dust.

Sarcoidosis

Def. It is a systemic granulomatous disease of unknown etiology characterized by T.cell abnormality with lymphopenia and infiltration of tissues with T cells.

↓

Noncaseating epithelioid granuloma in various organs with derangement of normal tissue architecture. There is giant cells within the granuloma (langhans) with inclusions e.g schaumann and asteroid bodies.

Immunologic defects:

- There is impaired cellular immunity characterized by a complete skin anergy to tuberculin and other common skin antigens.
- Humoral immunity is normal and susceptibility to infections is not increased.

C/P

1- Lung → manifestations of interstitial pulmonary disease e.g exertional dyspnea, cough with fine crepitations.
2- Extrapulmonary manifestations:

Heart
Cardiomyopathy with arrythmia and conduction defects

Skin
* Erythema nodosum
* Lupus pernio i.e. indurated blue purple lesions on the face, fingers and knees

Nervous system
* Bilateral Fascial Paralysis
* Space occupying lesion

L.N.++,
Liver ++
Spleen++
Parotid ++

Arthritis

Eye
* Retinitis, uveitis, hypertrophy of lacrimal glands
* Keratoconjunctivitis.

D.I
(It affects posterior pituitary gland)

Hypercalcemia
due to secretion of active vit.D. from macrophage

Kidney
Stones or calcification due to hypercalcemia

* Sacrocidosis may be presented with acute onset (giving rise to two syndromes): Erythema nodosum, acute arthritis and hilar adenopathy (**Lofgren's syndrome**), uveitis, parotid enlargement and facial plasy (**Heerfordt waldenstrom syndrome**).
* Insidious onset sarcoid presented mainly by respiratory manifestations with less frequent constitutional or extra thoracic manifestations.
* Pleurisy is uncommon in sarcoidosis.

Diagnosis:

1) X-ray stages
- → 0- Normal
- → 1- Bilateral hilar L.N. enlargement
- → 2- Interstitial pulmonary infiltrate + hilar L.N.
- → 3- Interstitial pulmonary infiltrate only.
- → 4- Fibrosis and honeycombing

2) ↑ S.Ca - ↑ ESR
3) Hypoxia (by blood gases) due to diffusion defect
4) Bronchoalveolar lavage (**BAL**) showing increase of lymphocytes (indicator of disease activity.
5) Transbronchial biopsy from lung showing non caseating granuloma
6) Gallium lung scan showing diffuse uptake.
7) High serum level of angiotensin converting enzyme (indicator of disease activity).
8) Tuberculin is -ve in 80% of cases (**anergy**).
9) Kveim test by intradermal injection of sarcoid extract leading to sarcoid like lesions after 4-6 wks.
10) Pulmonary function tests showing diffusion defect with evidence of restrictive hypoventilation.

Treatment:

Many cases remit spontaneously, corticosteroid administration is the principal treatment.

- The indications of treatment are:
  * Symptomatic lung disease
  * C.N.S. involvement.

* Eye lesions
* Hypercalcemia
* Cardiac involvement

- The usual therapy is prednisone 1 mg/kg/d for 4-6 weeks then slow tapering over 2-3 months, this regimen is repeated if the disease again becomes active. Cyclosporine may be useful in extrathoracic sarcoid not responding to steroids. Angiotensin converting enzyme and BAL (indicators of disease activity) are used for follow up.

Prognosis and outcome of sarcoidosis:

- Most patients with acute disease are left with no significant residual effects.
- 50% of patients have some permanent organ dysfunction.
- 15-20% of patients remain with active or recurrent disease.
- Death occur directly due to disease in 10% of cases.
- The mortality and morbidity are mainly related to the respiratory tract abnormality.

Q Pulmonary diseases of unknown etiology:

- Sarcoidosis.
- Good pasture's syndrome (see nephrology).
- Wegener's granuloma (see rheumatology).
- Histiocytosis x (see later).

Idiopathic pulmonary fibrosis or Cryptogenic fibrosing alveolitis

This disease previously called Hamman Rich $.

Causes Auto immune!?

- It usually occurs in late middle age.

C/P

- Interstitial pulmonary fibrosis (as before)

Investigations

* **X-ray** → Miliary shadows
* Respiratory. function tests showing diffusion defect with restrictive hypoventilation.
* Blood gases → as before.
* CT scan lung, lung biopsy.
* BAL showing mainly alveolar macrophages.
* Transbronchial biopsy as before.

Treatment:

* Steroids
* Cytotoxic drugs may be added if there is no response e.g azathioprine or cyclophosphamide.

Prognosis:

* The median survival time for patients is about 5 years.

Pulmonary Tuberculosis

Pulmonary tuberculosis is a chronic communicable disease caused by mycobacterium tuberculosis characterized by a necrotizing (caseating) granuloma as a tissue response to seeded organisms.

Types of mycobacteria

1- Mycobacterium tuberculosis, it causes most of cases of tuberculosis.

2- Mycobacterium bovis is endemic in cattle and spread to man through infected milk causing gastrointestinal tuberculosis.

3- Atypical mycobacterium (non tuberculous mycobacteria).

It leads to **+ve** tuberculin test.

It is common in immunopomromised patients, causing disseminated infection syndromes rather than tuberculosis in such patients.

ex. * M. Marinum * M. Kansasii

* M. Avium (important cause of pulmonary infection in patients with HIV).

Pathology

- Those at high risk of acquiring T.B.
  * Children * Contacts * Patients with silicosis
  * Immunocompromised patients * Living in overcrowding with poor housing
- Entry of the organism through respiratory tract through inhalation of infected droplets produced by the coughing or sneezing of infected individuals.

After entry into the lungs, tubercle bacilli are ingested by macrophages and transported to regional lymph nodes, then it may disseminate widely.

- The reaction of the body towards tubercle bacilli depends on the individual's hypensensitivty, resistance and whether those bacilli are first seen by the body or it is the second exposure so if:

First exposure (primary)
(in individuals lacking previous contact with tubercle bacilli)

↓

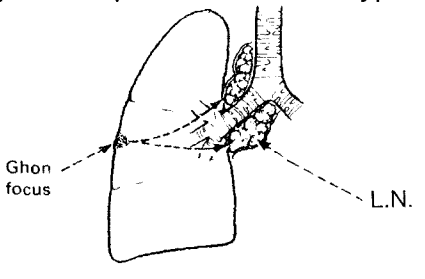
Primary complex

* Gohn's focus which is a single granulomatous lesion in the upper part of lower lobe or lower part of upper lobe.
* Lymphangitis
* Lymphadenitis (hilar L.N.)

Second exposure (post primary)
i.e in a previously sensitized individuals due to reactivation of dormant bacilli from primary lesions or due to reinfection

↓

The body develops resistance & hypersensitivity



Factors increasing the risk of tuberculosis:
- Children
- Close contacts of patients with positive smear for T.B.
- Primary infection < 1 year previously.
- Chronic lung disease
- Alcoholism
- Associated diseases e.g. silicosis, HIV, DM, CRF, liver cirrhosis, Lymphoma, Leukaemia, GIT disorders associated with malnutrition e.g. malabsorption disease.
- Patients under immunosuppressive drugs.

I. Pathology of primary T.B complex and its Fate

I- Healing → **Complete** resolution by fibrosis and calcification.

↓

incomplete (dormant Gohn's focus) i.e. healing for months or years then reactivation occurs, e.g. during periods of low resistance → Exacerbation

II- Hypersensitivity:
- Erythema nodosum.
- Phylectinular conjunctivitis
- Pleural effusion

III- Progression of primary complex (Gohn's focus and L.N):

Lymph nodes

↓

Enlargement → Middle lobe $ / Mediastinal $ / Pulmonary collapse

Rupture into → Pericardium → T.B Pericarditis / Pleura → pleurisy / Pulmonary vessel → miliary T.B.

Gohn's focus

↓

Progressive pulmonary T.B. **e.g.** T.B. pneumonia

II. Pathology of post primary T.B

The term post – primary TB is usually due to one of the followings:

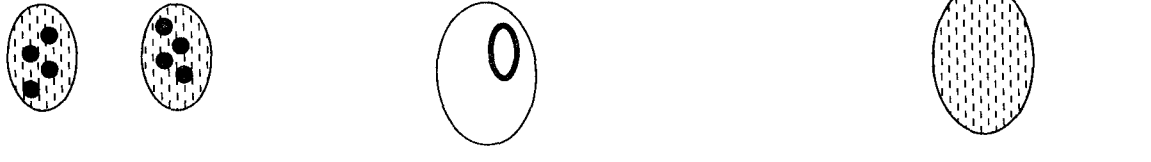
↓

- Reactivation of an incompletely healed primary focus
- Hematogenous spread from unhealed L.N.
- Re-infection

- Post primary tuberculosis is generally found in the apices of the lungs, reflecting the preference of M. tuberculosis for high O_2 levels, these lesions may progress to one of the following:

↓

T.B. bronchopneumonia | **cavitary fibrocaseous T.B.** | **Miliary T.B.**



C/P of TB

TB is usually classified as pulmonary or extrapulmonary. In absence of HIV infection, it involves the lungs only in > 80% of cases. In presence of HIV, up to 2/3 of patients with TB have either extrapulmonary disease alone or both pulmonary and extrapulmonary disease.

I- C/P of Primary complex (it is often seen in children)

In most cases the primary infection produces no symptoms or signs. Fever, dry cough may occur for 1-2 weeks so, the condition usually passed unnoticed unless the following investigations are done.

- Chest x-ray
- Sputum examination
- Tuberculin test shows conversion from **-ve → +ve**

So clinical disease results from the development of hypersensitivity or progression of the primary complex.

(A) Hypersensitivity: to tubercle bacilli may occur leading to:

a- Erythema nodosum
- * Bluish red nodule
- * Raised
- * Tender
- * Cutaneous on the skin of tibia
- * Tuberculin test is strongly **+ ve**

b- Pleural effusion → exudative reaction (Hypersensitivity)

c- Phylectinular conjunctivitis.

(B) Progression of primary pulmonary tuberculosis

G. features of T.B.	lung lesions	Bronchial	Miliary T.B	Dissemination
as night fever and sweating with loss of weight and loss of appetite. Cough haemoptysis May occur	↓ • Cavity • Pneumonia (especially right middle lobe) • Pleural effusion due to rupture of T.B Cavity into the pleura.	compresion by enlarging lymph nodes ↓ Collapse (especially right middle lobe)	(see later)	(see later)

- The lung lesions in primary T.B is usually localized to the middle and lower lung zones.
- The primary T.B may resemble bacterial pneumonia and should be especially suspected with history of close contact to a case of T.B.

II) Post primary T.B.

This occurs due to second exposure or reactivation of primary T.B as mentioned, it may presented by the following:

C/P

* G. features of T.B. → night fever and sweating,loss of weight and appetite
* Cough, expectoration
* Haemoptysis may result form

1- Bleeding from vascular tissue granulation

2- Erosion of big vessel traversing a tuberculous cavity

* Manifestations of pneumonia, cavity, milliary T.B. (see below) or pleural effusion

The lesion in post primary T.B is usually localized to the apical and posterior segments of the upper lobes.

Miliary tuberculosis

Manifestations:

- Fever, sweating during sleep, loss of weight.
- Cough and dyspnea.
- Wide spread crepitations may be heard
- Fundus examination may shows choroidal tubercules.
- It also affecting kidney and bone marrow.

Investigations:

- Chest x-ray showing miliary shadows.
- Tuberculin test is usually negative in the later stages of the disease.
- Bacteriological examination of sputum, urine or bone marrow.
- Blood picture, anemia and leucopenia may present.

Treatment:

- Anti tuberculous drugs.

An unusual presentation of miliary T.B seen usually in the elderly, it is called cryptic miliary tuberculosis.

Presentation of cryptic miliary T.B.

- Age over 60 years.
- Fever of unkown etiology and weight loss.
- Hepatosplenomegally in 25-50%.
- Normal chest X –ray.
- Negative tuberculin test.
- Blood picture showing leukaemoid reaction, pancytopenia also may occur.
- Confirmation by biopsy of liver or bone marrow.

Complications of pulmonary tuberculosis

1) Pneumothorax due to rupture of cavity in the pleural space.
2) Empyema or pyopneumothorax due to rupture of tuberculous lesion in the pleural space.
3) Tuberculous laryngitis.
4) Respiratory failure with extensive pulmonary destruction and fibrosis.
5) Fungal colonization of the cavities with asperigillus fumigatus (Aspergilloma)
6) Pulmonary fibrosis.
7) Constrictive pericarditis.
8) Tuberculous entritis follows swallowing heavily infected sputum.
9) Disseminated tuberculosis (tubercle bacilli gain access to the blood stream).
   a) **Miliary tuberculosis** with minute foci of infection in many organs particularly liver, bone marrow, spleen and kidneys.
   b) **Isolated organ tuberculosis** when disseminated organisms become established in only one or two organs most often adrenals, kidneys, bone or female genital tract (salphingitis, endometritis).

(The extrapulmonary sites or the lesions of disseminated T.B are):
- Adrenal →Addison disease
- Brain→ Meningitis with cranial nerve palsies.
- Peritoneum → T.B. peritonitis → ascities.
- Lymphadnopathy commonly at cervical and supraclavicular.
- Gatrointestinal T.B., The terminal ileum and caecum are common sites. This leads to abdominal pain, diarrhea and palpable abdominal mass.
- Bone→Osteomylitis and pott's disease.
- Bone marrow →Anemia and thrombocytopenia.
- Genitourinary T.B:
  - T.B. kidney → sterile pyuria.
  - T.B. epididymitis.
  - T.B Salpingitis or endometritis → infertility.

10) Side effects of anti tuberculous drugs.

Investigations

(T.B. is mainly a bacteriological diagnosis by **Ziehl-Neelsen** stained smear or culture on **Lowenstien Jensen Media or Middle brook).** The culture on middle brook needs short duration (2-3 wks) PCR is also a recent methode (see later).

1- Bacterial examination: If **-ve** for 3times, this may indicates **-ve** T.B infection!?
- Mycobacteria is recognized by their surface lipids which makes them acid fast in the laboratory examination.
- Isolation of organism from

Sputum, it can be induced by nebulised hypertronic saline if there is no expetoration | Fluid of gastric washing fluid e.g for children | Bronchial lavage fluid | Urine | CSF | B.M

2-Radiological picture: (usually gives apical lesion)

* Cavity	* Fibrosis	* Consolidation
* Effusion	* Collapse	* Miliary shadow

3-Tuberculin skin test:

- It is used widely to screen certain high risk populations, particularly those who have been exposed to an infectious patients.
- The test involves an intradermal injection of the purified protein derivative (PPD) of the bacilli.
- After 48-72 hours the injection site is examined for visible and palpable induration.
- Because of a possible cross reaction after exposure to other mycobacteria a single tuberculin test to determine sensitization to mycobacterium tuberculosis is considered positive only if the diameter of the induration at the skin test site measures:
  - ≥ 15 mm in immunocompetent individuals.
  - ≥ 10 mm in sick persons without depression of their immune system.
  - ≥ 5 mm in immunocompromised patients e.g (organ transplant recipients or patients with HIV infection).

Values of tuberculin test:

1. Positive test indicates recent or old infection or vaccination.
2. If it becomes +ve in a child, this mostly indicates recent tuberculous infection !?.
3. For contact with a case

Contact with **–ve** tuberculin	Contact with **+ve** tuberculin
↓	↓
Repeat after 6 weeks if- ve give BCG	Follow up (sputum, X-ray) if **-ve** give INH for one year (see chemoprophalaxis, **+ve** cases treated by antituberculous drugs as usual

4. A repeatedly negative test after 6 weeks from the onset of symptoms may rule out tuberculosis !?
5. Tuberculin test is also positive in atypical mycobacterium infection.
   . Specific PPD for (avium,kansasi) is the method to differentiate atypical mycobacterial infection from mycobacterium tuberculosis.

Causes of false -ve tuberculin test:

1- Before 6 weeks (preimmune period)
2- Immunocompromised patient **(anergy)** e.g. → AIDS → Cytotoxic → Steroids → Sarcoidosis
3- Bad technique
4- Miliary T.B 5- Viral infection e.g measles → immunosuppression.

4- E.S.R: → ESR ↑↑ in active T.B. (usually> 100)
→ It is used in follow up
→ Can rule out active T.B if it is normal !?.

5- Blood picture:

- Leucopenia with relative lymphocytes
- Anemia of chronic disease (normocytic, normochromic)

6- PCR: Recently it is an accurate technique(sputum – BM – CSF – urine).

7- Biopsy from the pleural, lymph nodes or solid lesion within the lung or from peritoneum, liver or bone marrow in disseminated disease:

Q DD. of T.B

1- Cases of pleural effusion
2- Cases with bronchopneumonia
3- Mediastinal lymph node enlargement e.g. sarcoidosis or lymphoma.
4- Coin shadow in chest x ray • Bronchial carcinoma, Bronchial adenoma
5- Miliary shadows in chest x ray
6- Fever of unknown etiology.

Medical Treatment:

1- Bed rest and isolation of patients who are excreting the organism

2- Good nourishment

3- Drugs:

Rules 1- Long course to avoid relapse
2- Combinations to avoid resistance (at least two antimicrobial agents)
3- Rifampicin → shorten the course of treatment to 9 months.
4- I N H must be used
5- Side effects of drugs must be known.

Drugs

- **I.N.H:** the most effective constant drug, it is bactericidal, it interferes with lipid and nucleic acid synthesis.
  Dose: 200-300 **mg/day** (5mg/kg)
  Side effects: hepatotoxicity, polyneuropathy. Pyridoxine 10 mg/d is given to prevent polyneuropathy.

INH is acetylated in the liver, so rapid acetylators are more liable to develop hepatitis due to the acetylated metabolite, however slow acetylators are more liable to develop neuropathy.

- **Streptomycin (Bactericidal):**
  Dose: 1**gm** I.M daily
  Main side effects: ototoxicity → irreversible
- **Rifampicin (Bactericidal, it inhibitis DNA dependent RNA polymerase) (10 mg/kg).**
  450-600 mg/d, it is hepatotoxic, it also causes vasculititis, hypersensitivity nephritis and flu like symptoms.

Rifamycins:

- Rifampicin
- Rifabutin, it is used to treat TB in HIV patients.
- Rifapentine, it is associated with more relapses.

- **Ethambutol ((Bacteriostatic inhibiting RNA synthesis)**
  10-25 **mg/kg,** it leads to optic neuritis
- **Pyrazinamid (PZA) (Bactericidal)**
  20- 30 **mg/kg**, **(**It may lead to hepatitis and hyperuricemia**)**

Surgical ttt

Lobectomy with resistant cases or recurrent haemoptysis.

Q Role of corticosteroids. In cases of T.B.

Indications = **1-** Miliary T.B !?.
2- Serous membrane affection to prevent fibrosis.
3- Replacement therapy if it leads to Addison's disease.

• Chemo prophylaxis of T.B.

INH for 6-12 months or INH and rifampicin for 3 months or pyrazinamid and rifampicin for 2 months can be given in non vaccinated contact who have recently tuberculin +ve, or in immunosuppressed contacts regardless the result of tuberculin. Infants of highly infectious mothers given in INH 5 mg/kg/d for 6 weeks.

Opinion:

- Tuberculin negative contacts, especially children should receive prophylaxis for 2-3 months and should be retested with tuberculin. Those whose results remain negative should discontinue prophylaxis.
- Contacts immunocompromised patients especially HIV patients and organ transplant recipients should receive a full course of treatment regardless the tuberculin results !?.

 # BCG (Bacille calmette - Guerin) (Attenuated M. bovis).

0.1 ml I.D at the junction of the upper and middle **1/3** of the upper arm. Its protective efficacy is up to 80% for 10-15 years and is greatest for preventing disseminated disease in children. It should not be used when there is known immunodeficiency. Tuberculin test can become positive after BCG administration.

Recent antituberculous can be used in resistant cases

- ♦ Capreomycin
- ♦ Clarithromycine
- ♦ Ciprofloxacine
- ♦ Cycloserine
- ♦ Azithromycine
- ♦ Ofloxacine.

Protocols or regimens of treatment

1- Nine month drug therapy:

Two months INH + Rifampicin	Then **7months**
± Ethambutol	↓
± Streptomycin	INH + Rifampicin

2- Six months drug therapy:

Initial **2m**	Then **4 m**
INH+ Rifampicin + Pyrazinamide	INH + Rifampicin
± Streptomycin.	
± Ethambutol	

3- Eleven months drug therapy: (12- 18m)

Twice weekly	**Daily**
Streptomycin 1gm. I.M plus	INH 300 mg and
INH **15 mg/kg + B6** orally	Thiacetazone **150 mg,** both drugs are given as a single dose by mouth

Q Response to treatment can be monitored by:

I- Monitor the response

- → Clinical improvement within 1-2 weeks.
- → Radiological improvement within 1 month.
- → Bacterial cure within 2-3 months (sputum conversion), it is the most reliable indicator of a response to treatment

II- Monitor the side effects of the used drugs.

- Pregnant patients should be treated as usual but PZA, streptomycin must be avoided.
- Patients with chronic liver disease can receive the usual treatment except (rifampicin), smaller dose of INH can be used.
- Patients with chronic renal failure can receive INH and rifampicine with the usual dose.
- Response to empirical antituberculous drugs usually seen after 1-2 weeks, this can be used as a therapeutic test for diagnosis of tuberculosis.
- Continued symptoms or persistently positive smears or cultures after 3 months of treatment should raise the suspicion of drug resistance or non compliance.

Cor Pulmonale

Definition

It is a right ventricular hypertrophy due to parenchymal lung disease, vascular lung disease or chest wall disease with or without right sided heart failure. So, there is secondary pulmonary hypertension due to the following causes.

Causes

1) Parenchymal lung diseases → Hypoxia.
   a.Chronic obstructive pulmonary disease. (chronic bronchitis/emphysema)
   b. Interstitial lung fibrosis
2) Vascular lung diseases
   a. Bilharzial cor pulmonale
   b. Thromboembolic P++ (subacute cor Pulmonale)
3) Chest wall diseases **e.g**. Kyphoscliosis → hypoventilation → hypoxia.
4) Disturbance in respiratory control
   - Morbid obesity (pickwickian$!?)
   - Sleep apnoea.

   } Hypoxia

Hypoxia → pulmonary arteriolar vasoconstriction → pulmonary hypertension.

C/P

1) Cause
2) Right ventricular++, pulmonary hypertension (see CVS)
3) Right ventricular failure → (see CVS).

Investigations

- ECG may be normal with emphysema or there is decreased voltage.
- Echo more accurate to diagnose Rt. V ++ or failure
- Investigation of the cause e.g. lung scan for pulmonary thromboembolism.

Treatment

- Treatment of the Cause.
- Treatment of right ventricular failure
  - Diuretics, vasodilators (ACE inhibitors).
  - Aminophylline
  - Digitalis (minimal role), you can give small dose as there is ↑↑ incidence of digitalis toxicity.
  - O_2 therapy e,g, in case of COPD and interstitial pulmonary disease.
  - Long term oral therapy with calcium channel blockers with high dose can reduce P++ e.g diltiazem 120-900 mg/dl (systemic hypotension may occur).
- Heart and lung transplantation is recommended for young patients.

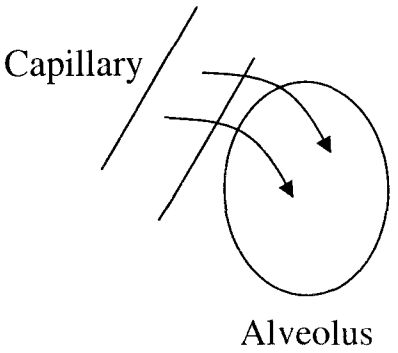
Adult Respiratory Distress $ (ARDS)

Definition It is a non cardiogenic pulmonary edema leading to acute respiratory failure (Type I respiratory failure). The term wet lung indicates, the presence of increased extravascular lung water.

Causes

1) Inhalation of irritant gases e.g chlorine, NO_2, smoke, ozone, high concentration of oxygen.
2) Gm -ve septicemia.
3) Fat, air, amniotic fluid embolism.
4) Pneumocystis carnii, viral pneumonia
5) Uremia, pancreatitis.
6) Immunologic response to host antigens e.g. Good pasture's syndrome, SLE.
7) Narcostic over dose e.g. heroin.
8) Aspiration e.g. gastric contents (**Mendelson's syndrome**), water with near drowning.
9) Disseminated intravascular coagulopathy (DIC).

Pathogenesis:



- One of the above causes acts as an insult to the capillary endothelium or alveolar epithelium leading to disruption of capillary integrity with extravasation of fluid, fibrin, RBCs and WBCs into the lung interstitium and alveoli.
- Tumour necrosis factor and IL-1 initiate the inflammatory response, these cytokines then stimulate IL-8 which perpetuates inflammation and coagulation.
- There is severe hypoxia, the lungs stiffen and become less compliant resulting in difficulty with mechanical ventilation.

- The pulmonary capillary wedge pressure is usually ≤ 18 mmHg with no evidence of elevated left atrial pressure, pulmonary hypertension may occur as the interstitial edema leads to compression on the blood vessels.

C/P Symptoms may develop immediately after the insult but usually are delayed for about 24-48 hours. There is progressive tachypnea, dyspnea followed by:

- Diffuse lung crepitations.
- Acute respiratory failure (diffusion defect) → Type I respiratory failure.

Notice the manifestations of the cause

Investigations

1) **X-ray** → Bilateral pulmonary infiltrates.
2) $PO_2 < 50$
3) Normal. heart (normal ejection fraction of the Left ventricle by echo), late, cardiac output decreased and be accompanied by metabolic acidosis and tissue hypoxia.

Treatment (Mortality > 50%)

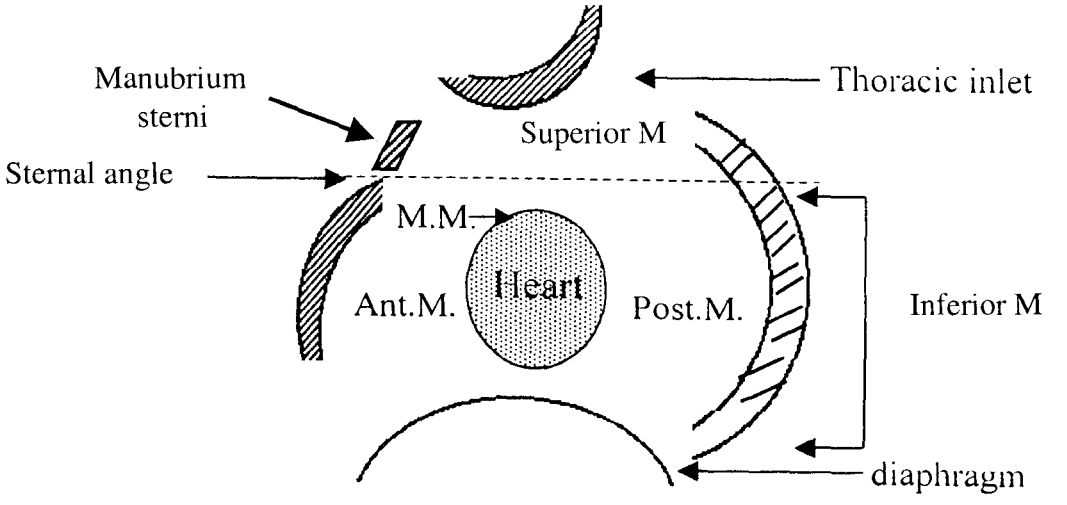
1) Cause
2) O_2 therapy with assisted ventilation PEEP (positive end expiratory pressure) to prevent alveolar collapse and increase lung volume. High frequency ventilation may be useful.
3) Steroids → improve capillary permeability!?
4) Diuretics !?
5) Inhaled nitric oxide and aerosolized prostacyclin may improve perfusion of ventilated lung units.
6) Surfactant replacement, TNF antibodies, ILI receptor antagonists and ketoconazole (inhibition of thromboxane synthesis).

Complications

- Pneumothorax and pneumomediastinum (due to ventilators) may cause abrupt deterioration in patients with ARDS.
- Secondary bacterial infection.

The Mediastinum and its diseases

Anatomy:



A- Contents of Superior mediastinum:

Nerves	Tubes	Vessels
• 2 Vagi	• Trachea	• Arch of aorta
• 2 Phrenic nerves	• Oesophagus	• Roots of big Vessels
• Recurrent laryngeal nerves	• Thoracic duct	• 2 Innominate Veins •SVC

B- Contents of Inferior Mediastinum:

Anterior	Middle	Posterior
• Thymus gland • Fat	• Heart, pericardium • Ascending aorta • Trachea and the main bronchi • Phrenic nerve. • SVC.	• Descending aorta • Thoracic duct • Oesophagus

(A) Mediastinal $ (Mediastinal mass)

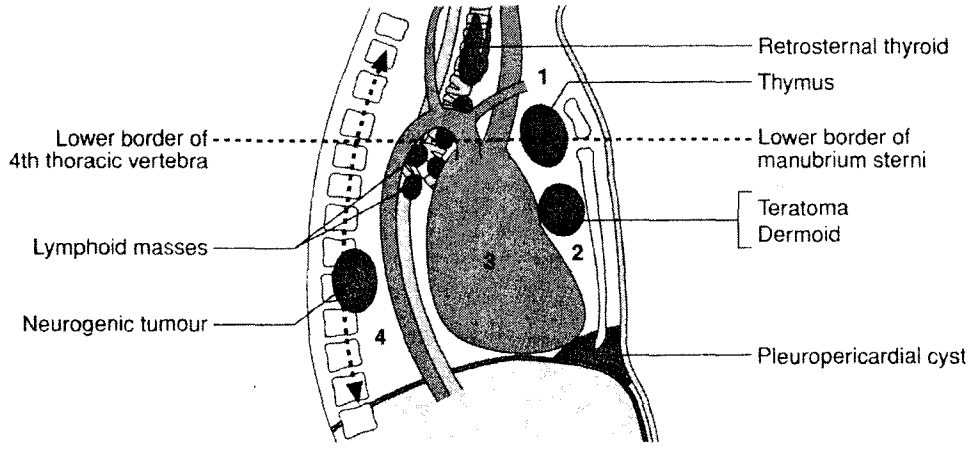
Group of clinical manifestations resulting from mediastinal compression & less commonly from pathological fibrosis within the mediastinum.

Causes: of mediastinal masses

- **Superior mediastinum**
  - Dermoid cyst
  - Thymoma
  - Retrosternal goiter, parathyroid tumors.
  - Aortic aneurysm
  - Lymphoma

- **Thymomas** presented with cough, chest pain and SVC obstruction. Myasthenia gravis occurs in approximately one third of patients, also pure red cell aplasia may occur, surgical excision is recommended.
- **Hodgkin's disease** and non Hodgkin's lymphoma rarely manifest as masses in the superior mediastinum.
- **Intrathoracic goiters** may occur in superior mediastinum, they usually are asymptomatic but may cause stridor, hoarseness or dysphagia.

- **Inferior mediastinum**
  - **Anterior M** → Dermoid cyst, pleuropericardial cyst, goiter or thymic tumor.
  - **Middle M.**
    - Pericardial effusion
    - Bronchial carcinoma
    - Lymphoma
    - Aortic aneurysm.
  - **Posterior M**
    - Hiatus hernia
    - Neurogenic tumours (Neurofibroma , pheochromocytoma)
    - Aortic aneurysm
    - Oesphageal tumours, lymphoma.



- Pleuropericardial cysts occur in the middle mediastinum at the right cardiophrenic angle appearing as smooth sharply demarcated masses.
- Neurogenic tumours are the most common tumours occur in the posterior mediastinum these tumours often are asymptomatic but may cause chest pain with steridor or cough. Horner's syndrome and spinal cord compression also may occur, examples of neurogenic tumours are neurofibroma and rarely **pheochrom ocytoma**.

C/P

Manifestations of the cause and features of mediastinal $ according to the site of the tumour or mass & the affected part of the mediastinum, the manifestations are due to compression on the following structures.

3 Tubes
- → Trachea → • Dyspnea, • Brassy cough
- → Oesophagus → Dysphagia
- → Thoracic duct → Chylous effusion.

3 Vessels
- → S. V.C. → • Oedema of the face, • Collaterals on the chest wall., • Congested non pulsating neck veins.
- → Azygos vein → Engorged veins on the upper part of the chest
- → Aorta → • Ischemic pain, • Inequality of pulse of upper limbs.

3 Nerves
- → • Left recurrent Laryngeal nerve → Hoarseness of voice
- → • Sympathetic chain → Horner's syndrome.
- → • Phrenic nerve → Diaphragmatic paralysis

3 Bones
- → • Ribs → Rib erosion with pain.
- → • Vertebra → Pain
- → • Sternum → Pain with aortic aneurysm

Investigations

1- Plain x-ray : Benign mass → Rounded with well defined border

Malignant → Irregular border

2- Fluoroscopy of the chest to diagnose

↓ Pulsating mass | ↓ Pleural effusion | ↓ Diaphragmatic movement

3- Left lateral view + Barium swallow

↓ Left atrial++ | ↓ Anterior mediastinal mass | ↓ Posterior mediastinal mass

4- Bronchoscopy & biopsy if needed.

5- Mediastinoscopy.

6- Scalene node biopsy.

7- Radioactive **I** uptake for thyroid swelling.

8- CT scan chest

9- Surgical exploration.

Treatment:

- Treatment of the cause

(B) Mediastinitis

(1) Acute mediastinitis:

It is a severe life threatening illness that most often follows rupture esophagus. It also may following endoscopy, dental work or other trauma. It is manifested by fever, chest pain with mediastinal enlargement. The disease progresses rapidly and requires emergency medical and surgical treatment.

(2) Chronic mediastinitis and mediastinal fibrosis:

Histoplasma, other fungi or mycobacteria may produce granulomatous process in the mediastinum, often with extensive scar tissue that contracts to cause narrowing of the trachea, bronchi, vena cava, pulmonary arteries and veins, chronic mediastinitis that occurs without any known cause is referred to as idiopathic mediastinal fibrosis.

(C) Pneumomediastinum

It is the presence of air in the mediastinum, air may expand into the neck tissues producing subcutaneous emphysema. If the mediastinal air is confined, the increasing pressure may interfere with circulation. When this occurs, tracheostomy is usually an adequate therapy. No intervention in patients without circulatory problems.

Bronchoscopy

The trachea & large bronchi are inspected by bronchoscope for the following indications.

Indications:

I- Diagnostic:

1- Structural changes or obstruction.
2- Bronchial brushings or washings **&** cytological examination of the aspirates especially for vascular tumor.
3- Bronchoalveolar (BAL) lavage to diagnose interstitial lung disease by examination of the aspirates for neutrophils, lymphocytes or eosinophils .
4- Transbronchial lung biopsy for sarcoidosis or other masses.
5- To determine site of haemoptysis.

II- Therapeutic

1- Removal of F.B.
2- Removal of secretions
3- Bronchial lavage in acute severe asthma !?

Complications

1- Infection. → pneumonia
2- Perforation.

Bronchography (old procedure)

Dye (Lipidol) instillated through nasal catheter or through the cricothyroid membrane to bronchial tree (now it is replaced by CT scan)

Indications → • To diagnose bronchiectasis
→ • Cystic lung disease

Complications → • Aspiration pneumonia.

Drug induced Respiratory disease

1- ARDS : • Streptokinase
• Opiates over dose • B2 agonist I.V

2- Opportunistic Infection • Steroid • Cytotoxic drugs

3- Interstitial lung disease:
- Amiodarone
- Nitrofurantoin

4- Cough → ACE inhibitors

5- Pleural diseases → SLE like with Phenytoin, Hydralazine, Procainamide.

6- Respiratory center depression → Sedatives, Opiates

7- Pulmonary eosinophilia → Penicillin, Sulpha, Gold, Penicillamine.

8- Bronchospasm → Aspirin, non selective B blockers.

Sleep Apnea Syndrome

A disorder characterized by repetitive periods of apnea (cessation of breathing) occurring during sleep. A period of more than 10 seconds without airflow is considered to constitute an apneic episode, patients with this syndrome can have hundreds of such episodes during the course of one night's sleep.

Types

1) **Central**: there is no drive for breathing during the apnea (no signal from the respiratory center to initiate inspiration).
2) **Obstructive**: transient obstruction of the upper airway usually the oropharynx preventing inspiratory airflow. The obstruction results from loss of tone in the pharyngeal muscles or the genioglossus muscle (which normally cause the tongue to protrude forward from the posterior pharyngeal wall).
3) **Mixed apnea**.

C/P Usually it is observed by the sleep partner.

* **Central** → No chest movement.
* **Peripheral** → Chest wall and abdominal movement can be detected during the attempts to move air through the obstructed airway with loud snoring.

Treatment

- **Central** → respiratory stimulant, phrenic nerve pace maker to stimulate the diaphragmatic movement.
- **Obstructive** → Avoidance of alcohol, sedatives and supine position, weight reduction, uvulopalatopharyngoplasty, tracheostomy

Complications:

Arrhythemia, P++, Unexplained cor pulmonale, sudden death.

Lung transplantation

Indications:

1- Pulmonary fibrosis
2- Primary pulmonary hypertension
3- Cystic fibrosis
4- Bronchiectasis
5- $\alpha_1$antitrypsin deficiency
6-Eisenmenger's syndrome.
7- Advanced COPD.

- Single lung transplant can be done in emphysema, pulmonary fibrosis, pulmonary hypertension.
- Bilateral lung transplantation is usually done in infective conditions to prevent spread of infection to the transplant
- Heart and lung transplant is done in Eisenmenger's syndrome and in cases of primary pulmonary hypertension.

- Donor selection includes age < 40 years, good cardiac and lung function and chest measurements slightly smaller than those of the recipient. ABO matching is essential.
- Immunosuppression with cyclosporine or tacrolimus, azathioprine or mycophenolate and prednisolone.

Complications of lung transplantation

1- Early post transplantation pulmonary edema, this requires diuretics, ventilator.
2- Infections
- Bacterial → Antibiotics
- CMV → Ganciclovir
- Herpes simplex → Acyclovir
- Pneumocystis carinii → co-trimoxazole.

3- Immunosuppression
4- Rejection • Early (first few weeks) → High dose **I. V** steroids
• Late (after 3 months) → High dose steroids may be effective

Histiocytosis X (Eosinophilic granuloma of the lung)

Def. Systemic disorders characterized by infiltration of lung tissue by non malignant histiocytes and eosinophils with fibrosis, it may be localized to bone or lung or it may be disseminated.

Pathology:

Proliferating histiocytes show cytoplasmic inclusions the so called x bodies.

C/P

- Cough
- Dyspnea
- Fever
- D.I.
- Exophthalmous
- Bony aches (bone lesions)

Investigations

- Bronchial lavage → X bodies.
- Bone X ray →bone defects.
- Chest x ray → Honey comb appearance.
- Lung biopsy is diagnostic

Treatment

- Steroids for pulmonary manifstations
- Radiotherapy for localized bone disease.

Eosinophilic granuloma of lung and bone including:
- Letterer siwe disease } Disseminated disease
- Hand Schuller Christian syndrome }

Oxygen therapy

Indications

1) Respiratory failure type I
2) Respiratory failure type III
3) Myocardial infarction
4) Crisis of sickle cell anaemia

Adverse effects (l00% O_2 is irritant and toxic)

- Retrolental fibroplasia and blindness in prematures if exposed to high concentrations.
- ARDS

So, do not use O_2 therapy except in indicated situations.

Administration

- High concentrations e.g. 60% via a mask used in acute Type I respiratory failure.
- Low concentrations either via a 24 or 28% ventimask in Type II respiratory failure.
- Continuous longterm domiciliary oxygen therapy for patients with advanced COPD or interstitial pulmonary fibrosis.

Mechanical ventilation

Patients with any type of respiratory Failure may require treatment with mechanical ventilation.

Types :

- IPPV (Intermittent positive Pressure Ventilation)
- PEEP (Positive End Expiratory Pressure), this prevents alveolar collapse during expiration and usually used in cases of ARDS. It also increases the lung volume. PEEP may cause barotrauma or a reduced COP. In patients with reduced COP the PO_2 increase but oxygen delivery to the tissue may decrease.

Chest wall disorders

Etiology:

1- Mechanical disorders e.g kyphoscoliosis, ankylosing spondylitis, obesity associated hypoventilation and chest wall trauma.

2 - Neuromuscular diseases e.g polyneuropathy, muscular dystrophies, spinal cord injuries and myasthenia gravis.

Chest wall disorders my cause respiratory dysfunction up to cor pulmonale and respiratory failure.

Kyphoscoliosis:

- This means posterior curvature (kyphosis) and lateral curvature (scoliosis) of the spine.
- The etiology is not clear in 80% of cases. A major known cause is childhood poliomyelitis, congenital abnormalities with or without bone defects are uncommon.
- Severe cases can lead to hypoventilation with dyspnea, hypoxia and cor pulmonale.
- Chest x-ray showing that ribs on the convex portion of the spine are widely spaced and rotated posteriorly causing a characteristic hump. Ribs on the concave aspect are crowded and displaced anteriorly.
- Early corrective intervention should be considered when the angulation is greater than 40 degree. The correction may be mechanical by a mikwaukee brace applied externally during the early stage of the disease or surgical correction by Harrington procedure.

Chest trauma:

(a) Blunt trauma causing rib fracture, hemothorax, pneumothorax and flail chest.

(b) Penetrating trauma causing puncture or laceration of chest wall and intrathoracic fistulae.

Bronchopulmonary aspergillosis

- Bronchial asthma
- Extrensic allergic alveolitis
- Pulmonary eosinophilia
- Intracavitary aspergillosis leading to haemoptysis

Eosinophilic pneumonias

- Eosinophilic pneumonias are composed of syndromes characterized by eosinophilic pulmonary infiltrates and peripheral blood eosinophilia.

Causes:

- Allergic bronchopulmonary aspergillosis.
- Tropical eosinophilia (filaria, ascaris, ankylostoma).
- Drug reactions e.g sulfonamides, penicillin, gold, penicilliamine and nitrofurantion.
- Loeffler's syndrome.
- Vasculitis e.g churg strauss vasculitis.
- Hypereosinophilic syndrome i.e presence of > 1500 eosinophils/ml for ≥ 6 m without any cause of eosinophilia with multisystem dysfunction (heart, lung, liver, spleen, brain).

C/P Fever – cough – dyspnea – wheezy chest

Investigations:

* Eosinophilia.
* Specific investigations for the cause.

Treatment:

* Treatment of the cause
* Steroids

Diaphragmatic paralysis

Causes

1- Trauma of phrenic nerve e.g surgery (Unilateral)
2- Compression of phrenic nerve by bronchogenic carcinoma, (unilateral).
3- Idiopathic (bilateral)
4- Viral infection e.g herpes zoster, poliomyelitis, it is usually unilateral, but may be bilateral.
5- Motor neurone disease, Guillain Barre$ and lesions of the upper cervical segments of the spinal cord → bilateral paralysis.

C/P → Cause

→ Bilateral:
- Dyspnea in supine position
- Paradoxical Abdominal movement
- Bilateral reversed tidal percussion.

→ Unilateral:
- No dyspnea
- Unilateral reversed tidal percussion.
- See-saw abdominal movement.

Investigations: It is suggested by chest x-ray and confirmed by fluroroscopy

ttt: Cause, night time assisted ventilation if bilateral or insertion of diaphragmatic pace maker.

Management of haemoptysis

Diagnosis:

1- History and physical examination to be sure that the source is pulmonary and not from the nasopharynx or GIT

2- Investigations:
- X-ray chest
- Sputum cytology and PCR for T.B
- Bronchoscopy
- CT chest
- Echocardiography for heart lesions
- ANCA for Wegener's granuloma.
- Antiglomerular basement membrane antibody for good pasture syndrome.

Treatment:

b) Minor haemoptysis → treatment of the cause

c) Massive haemoptysis (i.e. > 600 mg over 48 hrs)

- **Supportive care** → The patient should be positioned with the bleeding side in dependent position to reduce aspiration to the contralateral lung.
- **Definitive therapy:**
  1) Tamponade of the bleeding segment with a balloon catheter
  2) Endobronchial cold saline lavage.
  3) Embolization of the bronchial artery supplying the bleeding segment through pulmonary catheter.
  4) I.V vasopressine
  5) Surgical resection of the bleeding site.
- **Specific** treatment of the cause.

Causes Of Honey Comb Lung

- Bronchiectasis
- Sarcoidosis
- Cryptogenic fibrosing alveolitis.
- Neurofibromatosis.
- T.B.
- Asbestosis.
- Histiocytosis X.

Causes of lung cysts

- Congenital polycystic lung
- T.B
- Bronchogenic carcinoma
- Bronchiectasis + cystic changes
- Septic pulmonary infarction.
- Hydatid disease
- Staph pneumonia
- Metastases
- Lung abscess.

Causes of large bronchus obstruction

(1) Bronchial carcinoma (2) Bronchial adenoma (3) F.B.
(4) Secretions (5) Bronchostenosis (6) Aortic aneurysm

Partial bronchial obstruction → Infection, bronchiectasis
Complete obstruction → Lung collapse

Causes of solitary pulmonary nodules on chest x ray

- Bronchial carcinoma
- Sarcoidosis
- Rheumatoid nodule
- Adenoma
- Histiocytosis X
- F.B.
- T.B.
- Solitary metastases

Pulmonary vascular diseases

- Pulmonary embolism
- ARDS
- Bilharzial cor. pulmonale.
- Primary pulmonary hypertension
- Pulmonary vasculitis e.g. wegener's granuloma

DD of acute severe dyspnea

- Acute left ventricular failure
- Pneumonia
- Psychogenic
- Massive pulmonary embolism
- Pneumothorax
- Acute severe asthma.

Granuloma of the lung

A granuloma is a mass or nodule composed of chronically inflamed tissue formed by the response of mononuclear phagocyte system (macrophage / histiocyte) to a slowly soluble Ag. It is a chronic specific inflammation

Causes:

- T. B.
- Fungal
- Histiocytosis X
- Hypersensitivity pneumonitis.
- Sarcoidosis
- Wegener's granuloma

Lung involvement in systemic diseases

(1) Rheumatoid disease → Pleurisy, pleural effusion, caplan's $, and fibrosing alveolitis.
(2) Ankylosing spondylitis → Diminished chest expansion, interstitial pulmonary disease.
(3) SLE → Pleurisy, interstitial pulmonary disease and shrinking lung syndrome.
(4) Scleroderma → Pulmonary fibrosis and pulmonary hypertension.
(5) Wegener's granuloma → Haemoptysis, cavitation and pleurisy.
(6) Churg strauss $ → Asthma.
(7) FMF → Recurrent pleurisy.
(8) DM → Chest infection, TB lung.
(9) Myxedema → pleural effusion.
(10) Sarcoidosis, polycystic lung, histiocytosis x, HIV and α_1 antitrypsin deficiency are systemic diseases with lung involvement (see before).
(11) Liver failure → hepatopulmonary $
(12) Leukemias and lymphoma → Lung infiltration, mediastinal LN++ and pneumonia in immunocompromized patient.
(13) Renal failure → ARDS.
(14) Good pasture's $ → intraalveolar haemorrhage.

Extrapulmonary manifestations (organs involvement) of lung diseases.

(1) **Heart**: • Cor pulmonale with COPD, interstitial lung diseases and bronchiectasis.
• TB pericarditis in TB.
(2) **Liver**: Congestion with cor pulmonale, miliary TB affect the liver.
(3) **Kidney**: Amyloidosis occurs with bronchiectasis and chronic lung abscess. Miliary TB can affect the kidney, ureteric stricture may occur.
(4) **Blood**: Secondary polycythaemia with COPD and interstitial lung disease. Paramalignant $ of bronchogenic carcinoma.
(5) Endocrinal glands: • TB → Addisons disease.
• Paramalignant $ of bronchogenic carcinoma.
(6) **Nervous system**: TB → Pott's disease, cerebral tuberculoma. Paramalignant $ of bronchogenic carcinoma.
(7) **Skin**: TB → erythema nodusum, paramalignant $ of bronchogenic carcinoma.
(8) **Eye**: TB → phlyctinular conjunctivitis, chroid tubercules in miliary TB.

Sarcoidosis, polycystic lung, histocytosis X and α_1 antitrypsin deficiency are systemic diseases with involved lung, so you can enumerate their extrapulmonary manifestations.

Immune Mediated Lung Diseases

(1) Bronchial asthma.
(2) Interestitial lung diseases.
(3) Pulmonary vasculitis
(4) Graft rejection.

Pulmonary Emergencies

(1) Acute severe asthma.
(2) Acute respiratory failure.
(3) Tension pneumothorax.
(4) Pneumonia in immunocompromised patient.
(5) ARDS.
(6) F.B
(7) Massive haemoptysis.

Causes of persistent or chronic cough

(1) Bronchial asthma (cough variant asthma).
(2) Bronchiectasis.
(3) Bronchial carcinoma.
(4) Chronic bronchitis.
(5) Pulmonary tuberculosis.
(6) Repeated aspiration.
(7) Severe gastro-oesophageal reflux.
(8) Interstitial lung diseases.
(9) Drugs-especially ACE inhibitors.
(10) Psychogenic, including habit.

Systemic diseases causing wheezy chest

(1) Sturg strauss vasculitis.
(2) Sarcoidosis !?
(3) Carcinoid $

DD of wheezy chest

(1) Bronchial asthma (enumerate its types and triggers).
(2) Cardiac asthma.
(3) Eosinophilic pneumonia.
(4) Systemic diseases as above.
(5) F.B.

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